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ACUTE ABSCESS OF THE THROAT IN CHILDHOOD

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This report deals with 250 cases of true and potential, or abortive, abscesses in the throats of children under 14 years of age observed in the wards of the Children's Memorial Hospital, Chicago, over a period of ten years ended Dec. 31, 1940. In 181 of these cases there was frank suppuration, as shown by spontaneous rupture or surgical drainage. In the remaining 69 a localized inflammatory lesion, apparently differing in no way from the lesions in the early stages of the other group, subsided without evident pus formation for one reason or another. Nearly all of these cases were treated in the pediatric service exclusively except when laryngologic help seemed indicated as in any analogous situation. This rather unusual procedure requires some justification, at least an explanation.

At the Children's Memorial Hospital, except for one resident in pathology, all the house staff are future pediatricians or general practitioners and all of these rotate through the special as well as the pediatric services. In other words, there was no resident in laryngology to train for the practice of his specialty. Since the pediatrician and the general practitioner are obviously in the only strategic position to see the early stages of abscess formation, it is logically important that they should have adequate training in that direction. They have, moreover, from the nature of their experience a wider knowledge of clinical setting in general and of specific differentiation from other conditions with which an abscess might be confused than has the laryngologist who comes into the picture at, or near, the finish. To the experienced pediatrician this becomes evident as he scans the reports in the literature on this subject, nearly all of which come from laryngologists.

The pediatrician is a general practitioner who limits his practice to a certain age group, and it naturally follows that it may be difficult in a borderline situation to determine, to the satisfaction of all concerned, whether a given relatively minor case is logically and safely pediatric or, indeed, safely surgical. We feel that the simple abscess which constitutes the vast majority can safely be left in pediatric hands, while the more serious lesion, or complication, calls for the help of the laryngologist. Furthermore, except in case of hemorrhage from erosion of a prominent artery or of invasion of the mediastinum, both rare in childhood, or of those even rarer cases reported in the literature, which we have never encountered, in which a mere examination leads to sudden death, a fatality is nearly always due, not to the abscess itself, but to pulmonary, septic and other conditions in which the pediatrician is on more familiar ground than is the laryngologist. In all serious cases team work, at least, is indicated. The local lesion always has a child attached to it, and the child is often far more important than the local lesion. Finally, when Richards [1] in his authoritative paper on retropharyngeal abscess, after emphasizing the importance of a correct diagnosis and pointing out that 29 of his 162 cases were diagnosed incorrectly, comments "Mention of these errors is not in any way intended to cast aspersions on the diagnostic acumen of the examining physician, usually a pediatrician, but simply to call attention to the various deceptive signs and symptoms which this one single condition can present," one would seem justified, in the same kindly spirit, in considering this as further evidence of the need for more adequate training along these lines of the future pediatrician and general practitioner, who will eventually be called on, in nearly every instance, to stand in the first line of defense against such error in diagnosis. This view finds further confirmation in the following quotation from the same source: "Greenwald and Messaloff state that in their experience retropharyngeal abscess escapes recognition more frequently than any other acute disease in childhood. None of their cases came to them with this diagnosis but had been treated for from one to three weeks with no suspicion of the correct diagnosis. It is only fair, however, to state that the majority of these cases had not been seen by a laryngologist, who naturally would be more likely to detect the presence of an abscess." Because of the emphasis which we have always placed on the recognition of these abscesses, the errors in diagnosis on the part of our pediatric resident and outpatient staff were practically negligible.

Our purpose, then, is to present our observations from a pediatric point of view, in a simple clinical way, without anatomic or pathogenic detail, in the hope that they may be of interest and service to the pediatrician and general practitioner, and possibly to the laryngologist because of the method of approach.

From a purely clinical point of view we recognize three main types of acute abscess of the throat in childhood: retropharyngeal, retrotonsillar and peritonsillar, or quinsy. Parapharyngeal abscess will be considered as a complication, an extension, of one of these abscesses into the parapharyngeal space, or pharyngomaxillary fossa. Retropharyngeal abscess due to caries of the cervical spine does not belong in a discussion of acute abscess of the throat. No such abscess, moreover, occurred during the period covered by this series. While the differentiation between the different types of abscess

1. Richards, Lyman: Retropharyngeal Abscess, New England J. Med. **215**: 1120-1130 (Dec. 10) 1936.

is usually easily made, we have not always found it to be so especially in infancy. We have been compelled to record 8 as "uncertain" and we are not sure that our interpretation of the others is correct in every instance. We do feel sure that it is sufficiently accurate to make our statistical summaries as informative as if a few possible misinterpretations had not occurred. Because of our special interest in the subject, in the case of one of us extending over several decades, our own diagnostic and progress notes, as well as those of the house staff and the attending pediatricians and laryngologists, were more than usually full and adequate for our present purpose.

We have been impressed by the fairly constant chronological setting of the different types of abscess. Thus, the retropharyngeal abscess was almost restricted to the first two years of life; the retrotonsillar abscess came into prominence in the third and fourth years and tapered off after the seventh or eighth year; one peritonsillar abscess occurred in a child of 5 years, the rest from the seventh year on.

All of these acute abscesses have four cardinal signs or symptoms that vary in degree but are rarely absent:

1. An infection in the throat, preceding or concurrent.

2. Pain on swallowing. Children rarely complain much with an uncomplicated throat infection. If pain on swallowing, even to some extent without swallowing, supervenes on such an infection an abscess must be suspected. The pain is usually distressing, varying in degree with different types of abscess and naturally leads to a disinclination, even a refusal, to eat. It is promptly relieved if the abscess breaks or is drained surgically.

3. Localized swelling in the throat, the site depending on the type of abscess. This may or may not be visible; it can always be made out by palpation.

4. Unilateral, or predominantly unilateral, cervical adenitis on the affected side. Throat infections are commonly accompanied by pain, tenderness and swelling of the corresponding cervical lymph nodes, often to a pronounced degree. The adenitis tends, however, to be about equal on the two sides. A definite unilateral predominance, usually quite obvious to the eye, should always lead to suspicion of an abscess in the throat on the same side. Bilateral involvement of the cervical glands should occur with simultaneous bilateral abscesses in the throat, but this practically never occurs in childhood.

Other signs and symptoms of warning significance, such as noisy breathing with snoring and choking sounds; nasal, or mushy sound of the voice and cry; laryngeal obstruction with dyspnea, stertorous breathing and some cyanosis; regurgitation of fluids through the mouth and nose on swallowing; prominence of one tonsil or one side of the throat; deviation of the uvula away from an affected side, may occur to a varying extent with one or the other type of abscess. Their occurrence in the different types will be discussed under the appropriate headings. No significant relationship could be made out between the degree of fever and the severity of the illness, and no helpful prognostic information was obtained from blood counts. The fever ranged from near normal to 106 F. and the leukocyte count from normal to 82,000. In general both fever and leukocyte count ranged higher in the children with retropharyngeal abscess than in the others.

RETROPHARYNGEAL ABSCESS

A retropharyngeal abscess is a suppurative involvement, secondary to an infection in the throat, of one or more of three to five paired lymph glands that lie parallel to one another on each side of the posterior pharyngeal wall in the potential space between the prevertebral fascia and the posterior pharyngeal mucosa. These are said to atrophy after the third or fourth year, although "one or two remain on each side" (Lederle). It is generally assumed that this accounts for the fact that this kind of abscess is so rare after the period of infancy. If an upper gland is involved, or if there is an extensive abscess, this can usually be seen in the posterolateral angle of the pharynx. If the lower glands are involved they cannot usually be seen with ordinary pediatric technic; the palpating finger can, however, easily locate the swelling and can at the same time determine if fluctuation has occurred, and if so, to what extent. With such a low abscess there is now, in addition to the four cardinal symptoms, noisy, snoring, choking respiration, sometimes together with dyspnea and stertorous breathing as the larynx is impinged on. Cyanosis may occur but is rarely serious. The voice and cry are nasal and muffled in quality. Regurgitation through both nose and mouth may occur if the baby bravely attempts through hunger and thirst to overcome the handicap of painful swallowing. The tonsil is not pushed forward and there is no gross distortion of the throat as in the other types of abscess.

As in lymphadenitis elsewhere, suppuration may or may not occur. We did not, of course, attempt to determine the presence or absence of such involvement unless there were definite retropharyngeal symptoms. Of 105 cases of known retropharyngeal adenitis in our series, 23 subsided without apparent suppuration either spontaneously or following the administration of sulfanilamide; in 82 there was frank suppuration. Only the latter will be used for statistical purposes, as also in the other types of abscess. There was, however, no significant difference in the incidence as to the age of the child in the suppurative and nonsuppurative cases. Nearly 90 per cent of our 82 cases of retropharyngeal abscess occurred in the first two years of life, nearly 98 per cent in the first three years. Three of the infants were only 3 months old; one child was 3 years old and another 5 years of age.

RETROTONSILLAR ABSCESS

By retrotonsillar abscess we mean an abscess directly behind the tonsil in the lateral pharyngeal wall. In the literature this is sometimes included under "peritonsillar" abscess. The swelling may or may not be visible on simple oral examination, but it is readily made out by palpation. The latter too is the surest method of determining whether suppuration has occurred and to what degree. In addition to the four cardinal symptoms and signs there is another that is equally constant: the affected side of the throat is not only more prominent, an asymmetry that is nearly always signficant; the tonsil is pushed forward and mesially so that more of it is visible than of its mate. This is in striking contrast to quinsy, in which the swelling is mesial to and in front of the tonsil, so that the latter is pushed back and out of sight or nearly so. Children with retrotonsillar abscess are usually not as sick as are the infants with retropharyngeal abscess and much less so than older children with quinsy.

It has seemed to us that this type of abscess deserves more attention than has been given to it. In our series there were 79 cases with suppuration and 38 in which there was prominent localized swelling which subsided without drainage, either spontaneously or following treatment with sulfanilamide. There were thus only a few less than of the retropharyngeal type. We feel confident, however, that our interpretations were correct

except possibly in a few instances in late infancy. Only 2 occurred before the end of the second year of life. They were most numerous in the third and fourth years, about one half of the total number occurring during this period. After this they were fairly equally distributed up to and including the eighth year, after which they rapidly dropped to 4 in the ninth year, 3 in the tenth and 1 each in the eleventh and twelfth.

PERITONSILLAR ABSCESS

There were 11 cases of peritonsillar abscess, or quinsy, and 8 cases in which an initial swelling subsided either spontaneously or following the use of sulfanilamide. The youngest child with an abscess was 5 years old; the others were 7, 8, 9, 10 and 11 years of age, each year represented by two abscesses. This adds further support to the well known fact that quinsy is a rarity before the sixth or seventh year and that the incidence is low all during childhood as compared with that of other abscesses or with later life. In addition to the symptoms and signs common to all abscesses there is the obvious swelling, or bulging, mesial to and in front of the tonsil, causing the latter to recede and the uvula to deviate to the opposite side. A striking and characteristic sign, absent in all other kinds of abscesses of the throat, is the inability to open the mouth to more than a very limited extent, owing both to trismus from local conditions in the throat and to extreme pain when it is attempted. The rather prolonged course of the disease, the constant pain, the extreme dysphagia, the high fever, the loss of sleep, all lead to a severe degree of prostration and loss in weight.

PARAPHARYNGEAL ABSCESS

Only one parapharyngeal abscess was encountered. This will be discussed later.

EFFECT OF TONSILLECTOMY

In only 11 instances were abscesses found in children on whom a tonsil and adenoid operation had been done. Seven of these were retrotonsillar, 2 were peritonsillar and 2 were "uncertain."

DIAGNOSIS

The diagnosis of an abscess in the throat should rarely be missed if the condition is constantly in mind in the presence of any of the signs and symptoms that are so characteristic. Differentiation between the various types of abscess is sometimes difficult, especially in infancy and early childhood or if spontaneous rupture has occurred. In the great majority of cases it is not. In this series we were "uncertain" eight times for one reason or another. In addition to what has been said, two things may well be stressed: the diagnostic importance of palpation and the ominous warning significance of hemorrhage.

While certain abscesses can be seen, the palpating finger is always more revealing as to the location and, even more important, as to the stage of development. It is a simple procedure. It requires however a special technic, of which speed is an important factor. We have fortunately had none of those experiences which have been recorded, such as alarming symptoms, apnea and even death from the mere insertion of the finger or a tongue blade, although repeated examinations are usually indicated in order to note progress, and many more are made in a hospital for pedagogic reasons. Except for the toothless baby, some form of mouth gag is indicated if the finger is bare, and the pediatrician can feel more with a bare finger than with one that is covered by a rubber glove. A convenient and efficient mouth gag consists of two medium width tongue blades inserted on edge between the upper and lower maxillas in the region of the molars. This is more easily and readily removable and to us seems safer than the commonly used more cumbersome mouth gag. In examining for retropharyngeal abscess the moistened finger is rapidly passed over the tongue and down the pharynx. This method is probably the safer one but has the disadvantage of having the ungual surface of the finger next to the abscess. In larger infants the finger can safely be passed from above if too great force is avoided. This brings the palpating surface more naturally against the site of the abscess in the posterolateral angle of the pharynx. The examination must be made quickly without force, and care must be taken, if the finger is bare, that it is withdrawn before the tongue blades are removed. A bite in the presence of an infection in the throat is not without danger, as one of us can testify from personal experience. If there is a severe adenitis or an abscess, the normally concave posterolateral angle of the pharynx is obliterated on the affected side by a rounded protruding swelling. If fluctuation is present, it can readily be made out and also the degree to which it has advanced.

In palpating a retrotonsillar or a peritonsillar abscess, much the same technic is applied except that the finger is best inserted at the angle of the mouth on the affected side.

Frank bleeding supervening on an abscess in the throat must always lead to the suspicion of a parapharyngeal abscess with erosion of a large blood vessel, usually the common or internal carotid, although the vertebral artery may be the source of the hemorrhage, as in a case reported by Richards. Repeated pharyngeal hemorrhage practically establishes the diagnosis and makes the indication for surgical intervention imperative. There was only 1 case in our series, that of a boy of 7 years who died of a sudden massive hemorrhage.

PROGNOSIS

The outlook in throat abscesses in children is generally favorable, although there is a potential danger that must always be kept in mind. Death is rarely due to the abscess itself; more often it follows from an infection of which the abscess is a complication, not a cause. This is confirmed in our series. There were three deaths. Only one of these, the parapharyngeal abscess, was unquestionably due to the abscess itself. The other two followed retropharyngeal abscesses. One occurred in an infant of 7 months with "a low abscess encroaching on the larynx." The abscess was opened by one of the laryngologists, who reported obtaining about 2 drachms (8 cc.) of pus. Five days later he noted "Pharyngeal swelling practically all gone. Breathes normally." Two days later there was definite pneumonia, followed by a severe diarrhea, to which the infant succumbed twelve days after the abscess was opened. The necropsy report stated "Mucosa of pharynx intact. Small area of infection at site of abscess drainage. Mediastinum normal." This baby, moreover, had an eczema, a well known risk in any respiratory infection.

The second death following a retropharyngeal abscess was in an infant of 11 months with an extensive bronchopneumonia and an admission temperature of 106 F. There was so much obstruction to breathing that a tracheotomy was considered. There was "moderate

opisthotonos and a spinal fluid cell count of 66." A small abscess was opened by the laryngologic service. Two days later the following notation was made: "Retropharyngeal swelling has disappeared. Breathing is much easier." The temperature remained around 105 F. and the child was kept in an oxygen tent. Death occurred on the following day, obviously from an overshadowing bronchopneumonia. Although death could hardly be attributed to the abscess itself in either of these 2 infants they will be included in a statistical summary, as is usually done, because they died after a retropharyngeal abscess.

The total mortality of all patients with abscesses was 1.7 per cent; of those with retropharyngeal abscesses, 2.4 per cent. Statistics of mortality from any one source may be seriously misleading. The element of luck may easily play a major part. Thus, Richards reports a mortality of 7.4 per cent in 162 cases of retropharyngeal abscess. Luck was not with him, since of his twelve deaths two were due to hemorrhage, one from a carotid and one from a vertebral artery; one to an insertion of a tongue blade; one to a preliminary laryngoscopy, one to a mediastinitis; one occurred three hours after a spontaneous rupture and in four there was a generalized septicemia. He[1] reports the mortality following retropharyngeal abscess in the hands of others as follows: Frank in 1921, 6.7 per cent in a series of 74 cases; Babbitt in 1924, 10 per cent in 50 cases; Guthrie in 1926, 15 per cent in 20 cases; Greenwald and Messeloff in 1929, 7.3 per cent in 55 cases; Bokai 4.4 per cent in 317 cases; Wishart in a series of 41 cases had only one death and that in a moribund patient, a preoperative fatality. From all this it is evident that an abscess in the throat of a child must not be taken lightly and also that luck seems to have been with us in our series.

TREATMENT

The general treatment is much the same as that of any serious infection of the upper respiratory tract and need not concern us in this connection.

We feel very strongly that in the local treatment of any abscess of the throat, other things being equal, we should wait before establishing drainage until there is not only fluctuation but advanced fluctuation, or pointing. Healing occurs more promptly and more surely if the abscess has fully matured; there is probably less danger of systemic invasion, and the necessity of repeating the operation is reduced to a minimum. This attitude explains, at least in part, the high incidence of spontaneous rupture, which, even to us, is a bit surprising in retrospect. Except in the case of the child with a parapharyngeal abscess there was, however, no serious complication following spontaneous rupture, and in this instance the abscess had broken long before the child came under our observation. Frankly, however, we were often a little chagrined, but not worried, when this occurred, as we naturally believe that an abscess should be opened when it is ripe both for the child's sake and for the training it affords. This does not apply to retrotonsillar abscess as fully as it does to the other types, as will appear later. Of eighty-two retropharyngeal abscesses thirty, of seventy-eight retrotonsillar abscesses sixty, and of eleven peritonsillar abscesses six drained spontaneously.

When abscesses were opened surgically this was done routinely by the assistant resident in the service at the time. The forceps was used in every instance except in a few cases treated by the laryngologists with the scalpel. In the case of three retropharyngeal and one retrotonsillar abscesses, either for class demonstration or because of an ominous outlook, one of us (J. B.) assumed the responsibility. Five retropharyngeal and five retrotonsillar abscesses were opened by the laryngologists, in three instances with forceps and in seven with a scalpel. The five peritonsillar abscesses that were drained surgically were all done by the laryngologists with a knife. Anesthesia was not employed for several reasons: because it constitutes a hazard from local conditions in the throat, because there is commonly a concurrent respiratory tract infection, because of the danger of aspirating pus while the cough reflex is abolished or obtunded and, finally, because of the effect on the child of an anesthesia as compared with that of the momentary, relatively slight pain that goes with opening a ripe abscess through a thin walled, pathologic mucosa.

The retropharyngeal abscesses were treated with the child in the erect position. Snugly wrapped in a sheet he was seated with the legs free on the lap of one assistant, while another held the head and inserted two medium width tongue blades on edge, as a gag, between the upper and lower maxillas. Even more here than in the mere digital examinations we feel that there is less danger from the use of tongue blades than from the usually employed, more cumbersome, mouth gag, because they are so much more quickly removable, especially in an emergency. Facing the child, the operator inserts a moistened index finger over the root of the tongue, locates the point of maximum fluctuation and with the finger still in the throat quickly inserts a fairly sharp pointed forceps into the abscess and opens it slightly. The baby is immediately tipped forward and held in a horizontal position for a time so as to avoid aspiration of the first gush of pus. He is then kept in bed on his stomach or on one side for some hours. In only a few instances was it necessary to repeat the procedure, usually because it was done too early or the opening was too small. The subsequent course can readily be evaluated by the degree of relief of all symptoms and if necessary by digital exploration.

The whole procedure, from the time the tongue blades are inserted to the time when the infant is tipped forward need not, and should not, take more than five seconds, certainly not more than ten. This in itself has an appeal as compared with the more time consuming exaggerated prone, or Rose, position, apparently increasingly advocated by laryngologists. In this position, with the head extended backward the abscess is opened under direct vision with a knife, often followed by a forceps to widen the opening and by suction to minimize the danger of aspiration of pus. The pediatrician at least can see better with the end of his finger than he can with a laryngoscope and he doesn't trust himself with a knife in the throat of a struggling baby. There is, of course, no evidence available that either method carries a lesser mortality or morbidity than does the other. We feel too that if the child had a choice he would much prefer to face the ordeal in the erect rather than in the unnaturally constrained prone position, and, after all, the effect on the mind even of an infant must be weighed in the balance. The first gush of pus when the abscess is opened in the erect position adequately empties the cavity, and any danger of aspirating pus later has seemed negligible and would, after all, be about the same in the two methods of procedure. We are also inclined to think that the ragged

opening made with the forceps is less apt to close prematurely than is the cleancut opening made by a knife, thus calling for less frequent need for reoperation.

Approximately 76 per cent of the retrotonsillar abscesses ruptured spontaneously. This was not accidental; we allowed most of them to do so. They come to a head rather rapidly as a rule, have a thin walled covering and commonly rupture within a few days. There is usually not a very large amount of pus, and the children are only exceptionally as sick or in as much discomfort as are those with the other types of abscess. In older children, and nearly all of the retrotonsillar abscesses occurred well beyond the second year of life, there is a certain amount of psychic trauma that can be avoided if the abscess is allowed to follow its own course. We have had no occasion to regret pursuing this method of procedure. Only when things did not progress favorably, when the course was unduly prolonged or there was marked dysphagia or discomfort did we intervene surgically, nearly always with the forceps and in much the same manner as detailed under the treatment of retropharyngeal abscess.

To what extent nature will sometimes take care of things along devious routes was illustrated in the case of a child of 5½ years with an abscess back of the left tonsil. Mere pressure on the ripe abscess by an examining finger caused a copious discharge of pus to shoot for some distance from the left ear. On cleaning the ear canal and again making pressure on the abscess, one could see pus welling through an opening in the anterosuperior wall of the external auditory canal. Recovery followed without further treatment. There was no discharge into the throat at any time. This may have been poor surgery, but it does convey a lesson.

The course of a retrotonsillar abscess, both advancing and receding, can readily be followed by noting the degree of subjective symptoms, by the position of the tonsil and if necessary by palpation. Relief is often spectacular. An older child who can hardly be induced to swallow any supper will often eat a hearty breakfast if the abscess has broken over night.

True peritonsillar abscess, or quinsy, we were glad to turn over to the laryngologists, always with the hope that they would not operate too early or that it would rupture spontaneously. The old saying that if no pus was obtained there was "a relief from congestion" has, fortunately, pretty much gone into the limbo of discarded therapeutic attitudes. The characteristic inability of the child to open his mouth to a pediatrically workable degree and the uncertainty of hitting the abscess and nothing else, call for the special skill of the laryngologist. While it is desirable, per se, to await obvious pointing of the abscess, the distress and prostration are so great that intervention is often indicated as soon as definite fluctuation, or the spot at which pointing will occur, can be made out. That many of them, under favorable circumstances, will rupture spontaneously and safely is shown by the fact that more than half of those in this series did do so, i. e. 6 of 11 cases.

The course and treatment of the one parapharyngeal abscess that occurred in our series point, once again, to the fact that the rare lesion, as this is in childhood, is apt to be misinterpreted, or temporized with, especially when the only relief can come from a mutilating operation with potentially serious sequelae. The ominous, warning significance of a hemorrhage from an abscess of the throat, especially if repeated, can well be emphasized again. This boy of 7 years had had a sore throat for two weeks, high fever, predominantly unilateral cervical adenitis, pronounced dysphagia, some spitting of blood for two days and a petechial eruption on his legs and torso obviously due to sepsis. When seen by one of us in the outpatient department, cautious inspection showed an intense redness and a swelling and edema that nearly obliterated all landmarks. There was some bleeding. A digital examination was unfortunately made by one of the house staff with a resulting fairly large and rather prolonged hemorrhage, which subsided after a time. There was an unfortunate delay in resorting to surgery, not due to the laryngologic service. Nine hours after admission he was taken to the operating room for ligation of the common carotid artery. The pharynx was now filled with fresh and clotted blood. With the beginning of anesthesia a sudden profuse hemorrhage occurred and death came promptly before ligation could be undertaken. In retrospect it is obvious that the procedure should have been instituted at once, although the result would probably have been the same in the presence of an advanced sepsis. At necropsy there was found "a large perforation of the posterolateral pharyngeal wall below the level of the tonsil" and "a large erosion of the internal carotid artery." The parapharyngeal space was "filled with a large clot that could be lifted out of the abscess cavity. Cultures from the abscess and from the blood stream yielded a hemolytic streptococcus."

SULFANILAMIDE

It was during the period covered by this series that sulfanilamide came into use. It was the only drug employed, because in the earlier years it was the only one of the sulfonamides current and also because we thought that a hemolytic streptococcus was probably the active agent. The drug was administered to 15 children with retropharyngeal, 10 with retrotonsillar and 3 with peritonsillar localized inflammatory lesions that seemed likely to go on to suppuration. Of these, 7 retropharyngeal, 5 retrotonsillar and 2 peritonsillar lesions did not suppurate. These figures give an incidence of subsidence without abscess formation approximately twice that of the whole series. No deductions are, of course, justifiable from so small a number and in a condition so variable and uncertain. It is, however, our general impression that an abscess may be forestalled if sulfanilamide, or one of the later drugs, is given early enough and in adequate dosage. The limitations of what constitutes "early enough" are obvious and remain to be determined from future experience. We feel that, in the light of our present knowledge, one of these drugs is clearly indicated if suppuration does not seem to have taken place.

The evidence that these drugs have only an inhibitory action and should not be given if suppuration has occurred is more convincing than the evidence that they should be given in the earlier stages. We have seen an abscess inhibited twice only to recur later when the drug was stopped, unhappily prolonging the illness and the discomfort. Eight infants with retropharyngeal abscesses were given sulfanilamide. Five of the abscesses ruptured spontaneously while the drug was being given, one was inhibited but developed a full blown abscess five weeks later, one was drained surgically eight days and another three days after the drug had been stopped. Of five retrotonsillar abscesses, four ruptured while the drug was being given and the fifth

came to a head three days after it had been discontinued. One peritonsillar abscess subsided temporarily with sulfanilamide but recurred six weeks later.

SUPPURATIVE CERVICAL ADENITIS

A final word as to the treatment of suppurative cervical adenitis that may result from any of these abscesses: In 12 instances, or 6.6 per cent, of our series, suppuration occurred. The incidence was inversely proportional to the age of the child, one half of them occurring before the fifteenth month. Cervical abscesses developed following seven retropharyngeal, four retrotonsillar and one peritonsillar abscess, the last in the youngest child in the series with that type of abscess. In addition to the factor of age there seems to be a direct relationship between the length of time that it takes for the abscess in the throat to come to a head and the likelihood of an eventual cervical abscess. We feel very strongly that these abscesses should not be opened until there is not mere fluctuation but definite advanced pointing with a thin walled glossy covering of the abscess cavity. A 5 mm. incision, if possible in a crease of skin for cosmetic purposes, together with drainage by means of a strip of rubber tissue or selvage edge of gauze for a couple of days is usually all that is necessary. If indicated, the incision can be kept open a few days longer by means of a groove director inserted just beyond the opening or by mere digital separation of the edges. The resulting scar is sometimes hard to find at a later time, a not unimportant item in an exposed area especially in the neck; and, again, the child is spared the greater pain of an early incision, the more prolonged drainage and the greater number of dressings.

There was 1 case in our series, the only one of its kind we have ever encountered, in which there was a direct communication between a cervical and a retropharyngeal abscess. This infant of 12 months entered the hospital with both a retropharyngeal and a cervical abscess, the latter, if anything, more advanced than the former, a very rare occurrence. When the abscess in the throat was opened the cervical abscess collapsed, and when pressure was made on the latter pus could be seen welling into the pharynx through the opening in the retropharyngeal abscess. Things seemed to progress favorably, but it was deemed more judicious to drain the cervical abscess externally five days later. Recovery was uneventful. In the older literature, especially, the advisability of opening some retropharyngeal abscesses externally nearly always comes up for discussion. It is hard to imagine any indication for external drainage of an acute abscess unless there is, as in this case, a free communication between the pharyngeal and the cervical abscess.

SUMMARY

In a clinical study of 250 cases of true and potential, or abortive, abscess in children under 14 years of age there were 181 abscesses and 69 cases in which suppuration did not occur. There were 82 retropharyngeal, 79 retrotonsillar, 11 peritonsillar, 1 parapharyngeal abscess and 8 of undertermined classification. There were two deaths following retropharyngeal and one due to parapharyngeal abscess. The total mortality was 1.7 per cent; that following retropharyngeal abscess alone was 2.4 per cent. Only one death was unquestionably due to an abscess itself, the parapharyngeal abscess. Complicating cervical abscess occurred in 6.6 per cent of the series.

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THE INCIDENCE OF PELLAGRA IN OHIO HOSPITALS

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In the extensive medical literature there is no study which gives any comprehensive appraisal of the general incidence of pellagra. Such reports as are available come from public health reports, mortality statistics and figures for hospitalizations in areas where the condition has long been recognized as a menace to health. Furthermore, there is no indication of the prevalence of pellagra in regions of this country where it has not been studied intensively.

As a consequence, there seems to be a widespread impression that this type of deficiency syndrome is very rare in the Northern states and exists only as a provincial problem peculiar to the endemic areas of the South. Indeed, case reports indicate that it is considered an exotic disease except in subtropical climates. For a number of years we have been engaged in the intensive study of pellagra in both sections of the country and have collected data which dispel any uncertainty concerning the wide distribution of nutritional deficiency in representative cities in both sections of the country.

Two previous reports of pellagra in Ohio, while indicating the occurrence, gave no indication of its incidence.[1] A comparison of available figures drawn from published records of hospital admissions in several regions of the United States throws light on the frequency of pellagra in the so-called endemic and nonendemic areas. While such variables as standards for hospitalization and readmission, diagnostic alertness and availability of adequate interim treatment and dietary adjustment are not the same in different places, a study of pellagra admissions reveals some interesting facts about the problem of inadequate nutrition reflected by very ill persons requiring hospitalization and about pellagra occurring as a sequel of other diseases.

MATERIAL AND METHOD

This report deals with the initial admissions of patients with the diagnosis of pellagra in the Lakeside Hospital, Cleveland, and the General Hospital, Cincinnati, and a comparison with admissions to hospitals in other areas. The Lakeside Hospital is a private institution with extensive facilities for teaching and investigation. The Cincinnati General Hospital is a municipal hospital where all the services are arranged for teaching purposes. The patients were all seen by members of the house staff and attending physicians and, during most of the year, by the special group doing research in nutrition. We have restricted the study to first admissions because the interest in pellagra stimulated by the nutrition research workers may well produce an arti-

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Drs. V. P. Sydenstricker, J. M. Ruffin and D. T. Smith supplied figures for admissions used in the text and tables.

From the Department of Internal Medicine, University of Cincinnati College of Medicine and the Cincinnati General Hospital, Cincinnati, and the Department of Internal Medicine, Western Reserve University, and the University Hospitals, Cleveland.

1. Fischer, J. L.: Pellagra in the North, Ohio State M. J. **24**: 615, 1928. Hoerner, M. T.: Pellagra in Ohio: Fourteen Cases Occurring in Dayton, Ohio, During 1928-29, Ohio State M. J. **27**: 296, 1931.

ficial factor increasing admissions. This trend would be seen especially in subsequent entries which are excluded from the tabulations.

We have included only cases presenting pellagrous glossitis and bilateral dermatitis, because these diagnostic criteria have been used in the reports tabulated for comparison (table 3). Since we have emphasized the very early change in the mucous membranes of the mouth and tongue as a specific index of nicotinic acid deficiency, many patients are now seen and successfully treated at an early stage of deficiency before dermatitis has occurred. A few have been observed for a time without any specific antipellagric remedy, and these patients eventually developed typical dermal lesions. Even using these criteria we feel certain that we are still overlooking many persons with larval or subclinical pellagra and related vitamin deficiency disorders. Glossitis and dermatitis indicate severe deficiency, comparable at different places and periods of time.

On this basis we have selected the records of 113 cases observed in Cleveland from 1931 through 1935 and 128 cases from Cincinnati seen in the five years ended with 1939. Prior to the beginning of each period represented, there was no special study of pellagra in either hospital (tables 1 and 2). The Cleveland cases

TABLE 1.—*Incidence of Pellagra in the Lakeside Hospital, Cleveland*

	Year					
	1930	1931	1932	1933	1934	1935
Medical ward admissions	1,024	1,169	1,300	1,195	1,286	1,212
Cases of pellagra	2	16	18	28	29	18
Percentage	0.2	1.4	1.4	2.4	2.3	1.5

constituted 1.5 per cent of all medical admissions, and the Cincinnati cases 0.95 per cent. The yearly increase in the number of cases diagnosed at each hospital probably reflects the interest stimulated by the intensive study of nutrition. The figures may well be interpreted as a result of dissemination of diagnostic skill rather than an increase in incidence.

RELATED STUDIES IN THE LITERATURE

Cases of pellagra are classified as endemic, alcoholic or secondary, depending on the chief cause of the vitamin deficiency. Among the endemic are included those in which food fads, idiosyncrasies, such as vegetarianism, and some ill devised therapeutic diets figure as well as those in which it has not been possible to obtain proper food. In alcoholic pellagra the vitamin wants have not been satisfied because the beverage alcohol, the chief source of calories, ordinarily contains none and the diet does not make up the deficit. The term secondary pellagra includes cases in which the diet, satisfactory for the ordinary requirements of health, is inadequate when some disease obstructs the intake, accelerates the loss or raises the needs for the vitamin rich foods. The resulting pellagra is intrinsically the same whatever the manner of its origin.

There are several reports of hospital figures on pellagra in various Southern states prior to 1930, but data are not available for comparison with total hospitalizations. Boggs and Padget,[2] in a study of pellagra in the Baltimore City Hospital from 1911 through 1930 inclusive, found 102 cases in 16,572 admissions, an incidence of 0.68 per cent. There were a few more in the alcoholic class than either endemic or secondary subgroups. In many instances a number of factors could be considered as contributing to the failure of nutrition, but it had been possible to classify each case on the basis of the primary underlying cause.

TABLE 2.—*Incidence of Pellagra in the Cincinnati General Hospital*

	Year				
	1935	1936	1937	1938	1939
Medical ward admissions	3,173	3,169	2,440	2,293	2,482
Cases of pellagra	8	23	28	35	34
Percentage	0.3	0.7	1.2	1.5	1.4

Musser,[3] reporting on the pellagra admissions to the Charity Hospital, New Orleans, for the years 1925 through 1931, found 751 cases in a total of 237,570 admissions, or an incidence of only 0.31 per cent. These were for the most part endemic cases, but some fell into the secondary and alcoholic groups.

J. S. McLester[4] found that admissions for pellagra at the Hillman Hospital, Birmingham, Ala., represented 0.83 per cent of all admissions for the period from 1920 to 1933. These were largely endemic cases. Studies on a large number of pellagrins treated as ambulatory patients have been going on in the Nutrition Clinic of the Hillman Hospital for five years under the direction of one of us (T. D. S.) and although several thousand have been observed only a few were admitted to the hospital. It should be pointed out that these figures might indicate that pellagra is more rare in certain Southern hospitals than in those we are reporting. This is because pellagrins are not ordinarily admitted unless they are considered emergency cases in many Southern municipal hospitals. In former years, severe pellagra was considered hopeless and mild pellagra not a sufficient reason for hospitalization.

Two more series are available in Harris's textbook[5] on pellagra. These include the records of Sydenstricker[6] for a twenty year period at Atlanta, Ga., and those of Ruffin and Smith[7] for a ten year period at Durham, N. C. By additional information forwarded by these investigators, we have compiled the figures for the proportion which pellagra admissions bore to total hospital entries. For the Georgia clinic

TABLE 3.—*Reported Incidence of Pellagra in Seven American Municipal Hospitals*

Place	Period	Cases of Pellagra	Admissions	Percentage	Average Yearly Pellagra Admissions
Baltimore City Hospital	1911-30	102	16,572	0.68	5
Charity Hospital New Orleans	1925-31	751	237,570	0.31	125
Hillman Hospital (Birmingham, Ala.)	1920-33	...	.....	0.83	..
University of Georgia (Augusta)	1920-39	660	36,000*	1.8	33
Duke Hospital (Durham, N. C.)	1930-39	237	26,279†	0.9	24
Lakeside Hospital (Cleveland)	1930-35	111	7,186†	1.5	19
General Hospital (Cincinnati)	1935-39	128	13,557†	0.95	26

* Approximate. † Medical admissions.

2. Boggs, T. R., and Padget, Paul: Pellagra, Johns Hopkins Hosp. Bull. **50**: 21, 1932.

3. Musser, J. H.: Some Notes on Pellagra, Libman Anniversary Volume **2**: 877, 1932.

4. McLester, J. S.: The Nature of Pellagra: A Critique, Ann. Int. Med. **8**: 475, 1934.

5. Harris, Seale: Clinical Pellagra, St. Louis, C. V. Mosby Company, 1941.

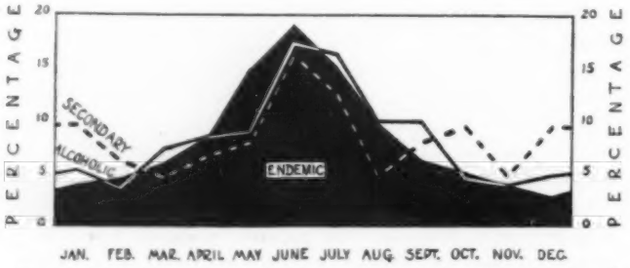
6. Sydenstricker, V. P., cited by Harris;[5] personal communication to the authors.

7. Ruffin, J. M., and Smith, D. T., cited by Harris;[5] personal communication to the authors.

there was an average of 33 pellagrins for 1,800 ward admissions for each of the twenty years. The incidence of pellagra was 1.8 per cent. The figures of Ruffin and Smith were correlated with admissions to the medical wards. For the ten year period ended in 1939 there were 237 admissions for pellagra among a total of 26,279 admissions to the medical wards, an incidence of 0.9 per cent. At the Duke Hospital only about half of the pellagrins seen in the clinic were admitted. These figures are tabulated for comparison with the Cleveland and Cincinnati groups in table 3.

The figures in table 3 may be compared with those given by Raman [8] for a general hospital in the Province of Madras, India. In this hospital it was found that pellagra accounted for 0.65 per cent of all cases admitted to the medical wards. This is only an indication of the worldwide prevalence of pellagra. Whenever this disease is sought, it is found among the debilitated patients of large hospitals.

From these figures we can readily see that pellagra is an important medical problem in all these hospitals. Furthermore, it is at once apparent that the disease is by no means confined to certain regions of the Ameri-



Monthly incidence of alcoholic and secondary pellagra as compared with endemic pellagra. The secondary and alcoholic groups are from this paper; the endemic group is taken from the report of Smith and Ruffin.[10]

can Southern states but is found in areas where it is not generally thought of as an important problem. The percentages are not comparable because the pellagra admissions are compared in part with medical admissions and in part with total hospital entries. This makes the figures compared with medical admissions appear high. In the Cleveland and Cincinnati figures, no cases of readmissions are included. This reduces the total number by about half. Nonetheless, one must conclude from these figures that pellagra is an important hazard in regions not considered to have a pellagra problem. The Ohio cases are preponderately secondary to organic disease or chronic addiction to alcohol, but many resulted from dietary restriction, whether obligatory, ill advised or wilful.

It must be emphasized that the number of cases in the tables indicate only a fraction of patients with vitamin deficiency. No persons with ariboflavinosis and neuritis are included. It was estimated by Goldberger that for every person with typical clinical pellagra there are from twenty to a hundred with varying states of inadequate nutrition. Even this proportion omits the vast number of people whose diet, though not actually deficient and responsible for no recognizable disease, is far from the optimum for best health and vigor. From our experience we can state that hesitancy to make the diagnosis of pellagra without the terminal triad of dermatitis, diarrhea and dementia has been costly in lives and has retarded understanding of the disease. In any vitamin deficiency state early specific therapy is more valuable than that which comes later when the disease is advanced and appears in its textbook form. From a careful review of prodromal symptoms observed for varying periods before the cases became well established, we are learning to recognize a nascent deficiency syndrome before any physical sign is manifest. For these reasons we have made surveys of the nutritional status of patients in the medical wards of the Cincinnati General Hospital. In spite of the extreme difficulty of obtaining reliable information about the past diet, a rough classification is possible. Preliminary studies indicate a high proportion of patients whose nutrition ranges from borderline to obvious deficiency. History of prodromal symptoms or objective manifestations of nicotinic acid, riboflavin or thiamine deficiency have been found in approximately 10 per cent of a series of 345 medical patients admitted to the wards for some other condition.

While alcohol addiction, particularly if complicated by cirrhosis, was a frequent cause, gastrointestinal, cardiovascular and pulmonary disorders were the most frequent predisposing causes. Acute infections were important in precipitating the development of clinical signs of vitamin deficiency disease. In almost every case there were several factors militating against adequate nutrition: previous inadequate diet, anorexia, fever, alimentary tract disorders, vomiting, diarrhea, liver disease, cardiac failure and many other circumstances. This reemphasizes the complicated substratum on which pellagra is engrafted and helps to explain some of the many vagaries of this disease.

SEASONAL VARIATION

It has been known for a long time that the incidence of outbreaks of pellagra rises in the spring to reach a peak in the early summer. We have therefore examined our material for the month of admission with pellagra, or the month of its detection if it developed in the hospital. Careful review of the histories reveals that clearcut evidence of glossitis or erythema appeared four to six weeks before admission in most cases. In the chart we have compared the percentage of each type classed as primarily alcoholic (169) and secondary (63) cases in this series with a table based on many thousand endemic cases compiled by Smith and Ruffin.[9] Our figures include the ten year period that ended with 1939, while those from Ruffin and Smith are for the first five years of the same period. Since the alcoholic and secondary cases from Ohio follow the same trend as the endemic cases from the Southern states, we believe that this reemphasizes the essential unity of pellagra of endemic, alcoholic or secondary origin first stressed by Spies and deWolf.[10] It also suggests that factors other than summer sunlight are important in this seasonal tide in pellagra.[11] Besides variation in food, it will be important to investigate such factors as fluctuations in metabolism, bodily activity and infections for their influence on the pattern of seasonal incidence.

COMMENT

In this study we have presented evidence that typical pellagra, the hallmark of advanced disproportion between nicotinic acid amide supply and requirement,

8. Raman, T. V.: Pellagra in India, Indian J. M. Res. **37**: 743, 1940.

9. Smith, D. T., and Ruffin, J. M.: Effect of Sunlight on the Clinical Manifestations of Pellagra, Arch. Int. Med. **59**: 631 (April) 1937.

10. Spies, T. D., and deWolf, H. F.: Observations on the Etiological Relationship of Severe Alcoholism to Pellagra, Am. J. M. Sc. **186**: 521, 1933.

11. Smith, J. H.: The Influence of Solar Rays on Metabolism, Arch. Int. Med. **48**: 907 (Nov., part 2) 1931. Sydenstricker, V. P., and Armstrong, E. S.: A Review of Four Hundred and Forty Cases of Pellagra, Arch. Int. Med. **59**: 883 (May) 1937. Smith and Ruffin.[9]

is a serious problem in two large hospitals in Ohio. While our figures are not suitable for exact comparison with other reports, it is obvious that pellagra is prevalent in Northern states. We believe that variations in its reported incidence depend on variations in recognition as well as true prevalence. Furthermore, clinical pellagra indicates advanced breakdown in nutrition. As the visible part of an iceberg, it may be the signal of widespread but subsurface danger in population groups under consideration.

In the present state of our knowledge, it is not possible for the practicing physician to derive much help in diagnosis from the complicated laboratory procedures used in nutritional research. Pellagra, beriberi and riboflavin deficiency have been found whenever an intensive search has been made in hospitals caring for large numbers of patients with serious disease. Secondary pellagra is recognized as a potential menace whenever familiarity with its early manifestations parallels careful clinical search for its presence where it is apt to occur. Unwise use of alcohol and ill advised diets used for reduction of obesity, treatment of peptic ulcer or control of diabetes frequently predispose to pellagra. While a careful appraisal of the history of dietary deficiency is still subject to many pitfalls, it should direct attention to the nutritional status of persons in whom it may be impaired. This is imperative wherever a combination of obstacles is placed in the way of proper nutrition. Any chronic illness or acute febrile disease, in addition to disorders of the alimentary canal, liver, heart and lungs which decrease available food when it is most needed, should be adequate warning of an impending deficiency.

Surgical operations on persons who have been suffering from some disease itself interfering with proper nutrition are apt to precipitate clinical signs of a deficiency syndrome. Shock, hemorrhage, anesthesia, nausea, vomiting, infection and fever, large quantities of parenteral dextrose and physiologic solution of sodium chloride, which not only increase carbohydrate metabolism but may effect a diuresis wasting vitamin stores, all oppose normal nutrition. Deficiency diseases may occur as an untoward sequel of operations under such conditions.

SUMMARY AND CONCLUSIONS

The data in this paper are presented as a progress note in a study of pellagra and related vitamin deficiency disease begun by one of us twelve years ago. It is at once apparent that pellagra is widely prevalent. For the two Ohio hospitals studied typical pellagra was found in 1 to 2 per cent of the medical admissions. This figure was doubled when readmissions were included.

The true incidence of pellagra appears to be underestimated. This is due in part to failure to suspect, to recognize and to report cases. Shifting emphasis toward the early signs of deficiency has revealed a higher incidence than that indicated by such studies as we report here.

Typical pellagra is the response of individuals to advanced or severe deficiency of the antipellagra factor. Such cases represent only a small proportion of persons whose inferior nutritional status is a handicap which may prove perilous in the presence of other diseases. This study does not include the large number of persons in whom malnutrition manifests itself as ariboflavinosis or neuritis.

PRESENT KEY PROBLEMS IN TUBERCULOSIS

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The sharpest controversy is now focused on three problems in tuberculosis:

1. Is a negative or a positive tuberculin reaction more desirable?

2. Are the lesions developing in recently exposed young adults of "primary" or "reinfection" type?

3. From what point should one date the clinical incipience of tuberculosis?

With regard to these three questions, it is in the first place to be emphasized that they have arisen only recently and are the result of the epidemiologic conditions which have developed in our midst within the last generation.

Previously in most communities it was true for the vast majority of persons that they become positive tuberculin reactors by the time they reached adolescence; that, while primary infections occurred in childhood, progressive pulmonary tuberculosis developed mostly only in early adult age; that a latent interval of a decade usually elapsed between the time of the infections and the evidence of progressive disease.

Only since the development of pulmonary lesions in tuberculin negative young adults has been observed in direct consequence of recent exposure has the question arisen whether these lesions are of primary or reinfection type.

Only since progressive disease following exposure and conversion from negative to positive tuberculin reaction has become a common observation has the question arisen. From what point should one date the clinical incipience of tuberculosis?

It is our contention that a rational answer can be given readily to these questions, but the answer will be different according to the epidemiologic environment in question. Failure to consider the factor of the epidemiologic environment is at the bottom of most of the misunderstanding and dispute over these questions. It is particularly true that there is lacking appreciation of the role of the epidemiologic environment in determining the character of tuberculous infections and the evolution of these infections in the majority of persons in the community in question.

This thesis will be best understood when applied to the discussion of the three key questions. Before entering on the discussion, to aid understanding, I present a brief review of the epidemiologic background of tuberculosis in the form of a table which speaks for itself. All we need to add here is a brief comment on the epidemiologic environment now prevailing in this country to which the present discussion is essentially applied. It is important to know that while the country as a whole has already gone ahead a long way on the downgrade phase of the epidemiologic cycle, there are sections, areas and racial groups within the country and in the midst of our communities still showing features of a high level of tuberculization. It may be said that in these "nests" (Frost) tuberculosis is still at its epidemiologic peak. The differences between some already greatly detuberculized and some still highly

tuberculized groups are now much accentuated in a manner which should be clear from the table and the discussion of the three key questions which follows.

QUESTION 1.—Is a negative tuberculin reaction more desirable than is a positive one?

ANSWER.—A negative tuberculin reaction is more desirable in a nontuberculized environment while a positive one is more desirable in a tuberculized environment.

REASONS.—*Facts.*—Tuberculosis is all the more serious a disease, the less prevalent tuberculous infections are in the community in question. Conversely, the more tuberculosis there is in a community the more are infections tolerated without producing disease.

The greater the number of negative reactors in the community, the greater the clinical significance of the fewer positive reactions, because a greater proportion of the latter will represent infections severe enough to lead to progressive disease. Conversely, in a community where the great majority are positive reactors the clinical significance of the latter is much less, relatively speaking, as the greatest proportion of such reactions represent only recurring contact.

Features of Three Epidemiologic Phases

	Upgrade	Peak	Downgrade
Community	Virgin	Tuberculized fully	Detuberculization; focalization
Mortality	Rising	Highest	Declining steadily
Morbidity	Rising	Highest	Declining steadily
Resistance	Low but rising	High	Beginning to decline
Allergy	Low but rising	High, prevalent and permanent	Declining incidence evanescent character resensitization
Contact	Increasing	Widespread and severe	Declining, particularly in severity and frequency
Infection	Rising incidence	Prevalent before adult age reached	Declining incidence particularly before adult age
Reinfection	None	None, hardly ever before middle age	Rising incidence throughout adult age
Disease	Acute and subacute generalized forms	Chronic endogenous phthisis and chronic hematogenous forms	Chronic exogenous phthisis
Latency	Infrequent, short	Prevalent and long between primary and chronic pulmonary tuberculosis between bouts of hematogenous dissemination	Declining and shortening between primary and chronic pulmonary tuberculosis

Contact is always dangerous to tuberculin negative adults because these are presumably coming from a nontuberculized environment. The danger is particularly serious if contact occurs in a highly tuberculized environment (tuberculosis institution, homes of patients with open tuberculosis). In adults who have grown up in a tuberculized environment a positive tuberculin reaction is a sign of an infection long overcome and hence an asset.

It should be remembered, however, that in very young adults a positive tuberculin reaction may be a sign of only recent first infection the outcome of which is still unsettled. There is evidence that added exposure during this early phase of the infection is not healthful and may be harmful.

Interpretations.—In highly tuberculized communities the opportunities for exposure are so constant and ubiquitous that everybody is infected already in childhood and continues to be exposed to reinfection throughout life. Universally the first infection is severe. In most cases it is enough to give permanent allergy. In a relatively small proportion of persons in the community as a whole, but in a considerable total number of people, the first infection is severe enough to leave lesions which remain susceptible of reactivation under the various exigencies of life, which is the so-called endogenous reinfection tuberculosis. Morbidity and mortality from the disease are high in such a community but the fatality of tuberculosis, considering the prevalence of this infection, is low. There prevails obviously very strong resistance to tuberculosis which is manifestly based on properties acquired by the first infection, which includes allergy. The vast majority of tuberculin positive reactors are safe in such a community.

Tuberculin negative individuals are safe only in a highly detuberculized community, where they may long remain uninfected or where infections are of a very much less severe type. Severe type of exposure is liable to become rather harmful to tuberculin negative individuals. Recent observations have demonstrated that a larger proportion of tuberculin negative adults so exposed will develop progressive lesions than is the case with already tuberculin positive individuals. It has been a long established fact that boys or girls who come from less tuberculized rural sections and become overexposed in a highly tuberculized city often develop disease. In the new epidemiologic environment we are dealing essentially with the same phenomenon in a somewhat different form and wider scale.[1]

QUESTION 2.—What is the character of the lesions that are developing now in recently exposed young adults? Are we dealing with "primary" or "reinfection" type lesions?

ANSWER.—In some instances we may be dealing with a truly first infection lesion. In other instances we may be dealing with lesions due to a recurrent infection. Both of these may have some features of a "primary" type yet follow the course of "reinfection" type tuberculosis; hence they cannot be told apart.

REASONS.—*Facts.*—True adult "primary" infections of identical course with childhood primaries ending up in calcified residues of the classic Ranke complex are not at all uncommon now when first infections have become postponed into adult age. "Primary-like" lesions produced by recurrent infections following evanescence of a preceding mild infection and its allergy are also quite common now. These too often end up in a residue which is in no way different from the classic calcified Ghon focus.

Progression to chronic pulmonary tuberculosis may occur now from truly "primary" but more often from the just described "primary-like" lesions, both of which represent exogenous fresh invasions.

Interpretations.—Under the present epidemiologic conditions a negative tuberculin reaction no longer indicates a noninfected state. Lesions arising after recent exposure in tuberculin negative individuals may now represent either true "primary" or "primary-like" recurrent infections. Not only is it impossible to tell these apart but there seems to be little reason for such separation.

In the first place our observations indicate that even recurrent infections with "primary-like" lesions may proceed to chronic phthisis not directly from the initial

1. At this juncture may we point to our prediction (THE JOURNAL, Oct. 12, 1940, p. 1295), on the basis of the foregoing considerations, that a rise in tuberculosis mortality will soon have to be faced in this country. The current statistical data already available indicate clearly such a trend becoming manifest first in the greater population centers.

exogenous focus but rather indirectly from the lymphohematogenous secondary foci in the apical and subapical portions of the lungs. Then it is conceivable that in the present epidemiologic phase even true first infections might produce "reinfection type" rather than "primary type" tuberculosis. This is just what Israel and his co-workers have recently assumed.

If I understand these workers of the Phipps Institute correctly, they advocate the revolutionary step of discarding altogether the concept of "primary tuberculosis" built on the enormous amount of experimental pathologic and clinical work of two generations since Parrott, Kuss, Ghon and others. Current observations led these workers to the following three interpretations: 1. Tuberculous first infections, which occur now mostly in young adult life, rarely produce primary type lesions. 2. Young white adults of this country respond to first infection with reinfection type lesions. 3. The response to tuberculous infection is determined by the character of the individual resistance and not by the presence or absence of previous infection.

The last explains the first and second points of this concept, which may probably be best described as an immunobiologic explanation of the current changes in tuberculosis. Undoubtedly this concept has been inspired by the results of Lurie's experimental work, which has emphasized the role of natural resistance in determining the character of the infection.

The concept presenting epidemiologic causes for the changing features of tuberculosis is less revolutionary, more simple and yet far reaching.

That the character of infections should change with the changing epidemiologic cycle has been a long emphasized fact. It is expressed in the general concept that the character of the epidemic determines the character of disease in all infections. It stands to reason that tuberculosis is no exception to this rule. Indeed, Frost years ago sufficiently emphasized the changing aspects of the tuberculous infection with the shifts in the epidemiologic environment. The latter we believe is a more logical explanation of the currently observed changes in tuberculosis. Point for point the logic of the latter concept as against the former might be stated as follows:

1. In the first place it is more logical to assume that "primary complexes" have become too mild, transient and inaccessible to clinical demonstration than to say that they no longer occur. As a matter of fact there is direct proof of increasing mildness of "primary complexes" already in the past. The rising incidence of evanescent tuberculin reactions in recent years indicates their complete obsolescence.

2. In the second place, it is hardly logical to insist on the "reinfection type" character of any tuberculous lesion now when distinction between the "primary" or "reinfection" type is admittedly no longer possible.

3. Finally it seems more logical to assume that recent rapid shifts in the epidemiologic conditions have had a more profound effect on the incidence and conditions of exposure than on individual resistance. We readily concede that in the present epidemiologic cycle people evince more natural resistance but postulate that primary infections have become more obsolescent because the conditions of exposure have materially changed.

QUESTION 3.—From what point should one date the clinical incipience of pulmonary tuberculosis?

ANSWER.—In very acute tuberculous processes the point of clinical incipience may readily be fixed to coincide almost with the time of first infection.

In very chronic tuberculous processes the clinical incipience cannot be fixed even with the appearance of the first demonstrable lesion.

REASONS.—*Facts.*—Tuberculosis is a process the evolution and pathogenesis of which differ with the character of the infection, which in turn changes with the epidemiologic conditions. In the epidemiologic upgrade phase the process is so rapid that it may be said to begin with the first invasion of the bacilli and their beginning multiplication at the site. At the epidemiologic peak the process is still set in motion by the first infection, but its evolution is so insidious that between the infection and the first clinical symptoms the period of latency may be one of years or even decades. Finally in the epidemiologic downgrade phase the process may require more than one infection to set it in motion and the evolution period shows the widest range from a few weeks to many years.

Interpretations.—Whether it is more logical to date the onset of pulmonary tuberculosis from the time a healthy person has first begun to react to tuberculin than it is to date it from the time a lesion has first become demonstrable by x-ray examination in his lungs will depend on age and place. This refers to the age of the person and the epidemiologic environment from which he comes and is living in. In persons reared and living in a highly tuberculized environment a positive tuberculin reaction is only to be expected. Here x-ray lesions are more often only potential and by no means definitely established phthisis. The vast majority of such lesions found in people in such an environment are definitely known to undergo more or less complete resolution and ultimate healing without ever producing clinical disease.

In persons coming from a highly detuberculized environment a positive tuberculin reaction may at times mark already the onset of disease. More often, however, there is a latency period of variable length during which presence or absence of a demonstrable lesion in the lungs is no criterion for the time of onset of phthisis. On one extreme there will be cases with such acute clinical onset that even the first positive roentgenogram shows already too extensive involvement. On the other extreme there will be cases in which the lesion first becoming demonstrable in the lungs remains for many months or years unchanged until finally its breakdown gives rise to progressive phthisis very abruptly.

The practical significance of the foregoing may now be stated as follows:

1. The younger the individual and the more detuberculized the environment, the greater the clinical significance of a positive tuberculin reaction and the phthisical potentiality of x-ray lesions.

2. Young people attending tuberculous patients must be very closely watched. Tuberculin negative persons are especially in danger. Even the tuberculin positive persons, if young, may have become positive only very recently and therefore are still not out of danger.

3. Since one cannot now tell apart the primary from the reinfection type lesion, all newly discovered x-ray lesions in young adults must be treated as potential phthisis, i. e., by a period of observation under rest.

4. On the individual himself and the local epidemiologic conditions must depend in each case determination of the point from which a newly arisen positive tuberculin reaction should be considered merely a sign of infection or an indication of clinical tuberculosis in need of treatment.

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AN EPIDEMIC OF COCCIDIOIDAL INFECTION (COCCIDIOIDOMYCOSIS)

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An epidemic of coccidioidal infection would have been inconceivable five years ago. Then the usually fatal coccidioidal granuloma was the only recognized form of infection by Coccidioides immitis. During 1936-1938 Gifford [1] and Dickson [2] proved that this fungus more frequently produces mild infections. Many of us are still conditioned by the former conception of coccidioidomycosis as a deadly disease. We hope that the record of this small epidemic will emphasize the frequency and usually benign character of coccidioidal infection in its endemic areas.

These endemic regions are, like the site of our small epidemic, semiarid with hot, dry and dusty summers and autumns. The most publicized is the San Joaquin Valley, the southern component of the great central valley, of California. Other parts of southern California, Arizona, Texas and probably New Mexico and Mexico are endemic centers. Sporadic cases have been reported elsewhere in North America and Europe. The only other known endemic area is the dry Chaco region of South America. Many investigators have associated these dusty, arid qualities with the theory that the infection is generally acquired by the inhalation of Coccidioides chlamydospores. These spores, which develop in the mycelial form of the fungus, are extremely infectious. The fact that coccidioidomycosis does not pass directly from host to host [3] indicates that the endosporulating spherules, characteristic of Coccidioides in man and animals, are not well adapted to disseminating the infection. These deductions explain other features of the epidemiology of acute coccidioidomycosis such as the maximal incidence in the dusty season,[3] the rapidity with which the infection is acquired [3] and the ultimate infection of more than three quarters of the long time residents.[4] The previous recovery of Coccidioides from one set of samples of San Joaquin Valley soil [5] is convincing corroborative evidence. The epidemic described here summarizes this entire epidemiologic concept.

The protean symptomatology of coccidioidal infection is also illustrated in this outbreak. We now recognize that the symptoms of an initial infection are variable. Cases are usually diagnosed "flu" or "bronchitis," although many rarer diagnoses are also made.[3] In from 2 to 5 per cent of such patients erythema nodosum and/or erythema multiforme develops, a symptom complex known colloquially as "San Joaquin fever," "valley fever," "desert fever" or "desert rheumatism."

This first reported epidemic of primary coccidioidomycosis involved 7 out of 14 Stanford University students and faculty members. On the afternoon of April 26, 1940 this group of 10 graduate and undergraduate students together with 4 faculty members left the Stanford campus on a biology field trip to San Benito County, Calif.

San Benito County is 100 miles southeast of San Francisco astride the Coast Range Mountains. While many parts of the county are well watered and produce diversified crops, those portions on the eastern slopes are quite dry. The Panoche Valley, separated from the San Joaquin Valley only by a low range of hills, averages but 8 inches of rain a year. In the spring the region is suitable for grain raising and grazing, though in the hot parched summers and autumns the country is sere.

The first night the party camped near the highway south of Hollister, the county seat. The following day was devoted to scouring the hills and valleys and collecting a variety of specimens: insects, arthropods, reptiles, flowers and plants. The night of April 27 was also spent in the open in the San Carlos Mountains, part of the Coast Range. On the following day the group returned to Stanford University.

On May 6, O. C., a graduate student aged 21, felt feverish and weak but had little malaise. He tried to overcome his indisposition with strenuous workouts. However, his illness grew worse and on May 8 he reported to the Men's Health Service. Because of a temperature of 103 F. he was hospitalized by one of us. A roentgenogram of the chest, taken because of some suspicious "tinkles," revealed multiple circumscribed densities. Various diagnostic tests including blood cultures, sputum examinations and cultures, serologic tests and coccidioidin tests were performed but failed to reveal the cause of the illness, although 10 mg. of coccidioidin produced some erythema with induration.

In the meantime five of the other students became ill: R. R. also on May 6, A. S. on May 7, D. S. and W. G. on May 10 and B. M. on May 11. All showed roentgenologic evidence of pulmonary consolidation or other pathologic process. Tests with 0.1 mg. of coccidioidin on 2 (A. S. and D. S.) were faintly positive and on B. M. strongly positive. However, examinations of the sputum were incomplete and the cause of the epidemic remained unknown.

The condition of all except the first patient (O. C.) gradually improved. He failed to respond to treatment, continued to have a high fever and his roentgenograms [6] appeared worse. On May 24 he was moved to the Stanford University Hospital in San Francisco for further diagnostic study. A test with 0.1 mg. of coccidioidin was repeated on May 26 and produced definite induration measuring 12 by 12 mm. in twenty-four hours. Gastric lavage was performed the day that the coccidioidin test was seen to be positive and a few suspicious spherules were seen. (Coccidioides immitis

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1. Gifford, M. A.: San Joaquin Fever, Annual Report Kern County Health Department for the Fiscal Year July 1, 1935 to June 30, 1936, pp. 22-23. Gifford, M. A.; Buss, W. C., and Douds, R. J.: Data on Coccidioides Fungus Infection, Kern County 1901-1936; Annual Report Kern County Health Department for the Fiscal Year July 1, 1936 to June 20, 1937, pp. 39-54. Dickson, E. C., and Gifford, M. A.: Coccidioides Infection (Coccidioidomycosis), Arch. Int. Med. **62:** 853-871 (Nov.) 1938.

2. Dickson, E. C.: Valley Fever, California & West. Med. **47:** 151-155 (Sept.) 1937. Dickson, E. C.: Coccidioidomycosis, J. A. M. A. **111:** 1362-1364 (Oct. 8) 1938. Dickson and Gifford.[1]

3. Smith, C. E.: The Epidemiology of Acute Coccidioidomycosis with Erythema Nodosum ("San Joaquin" or "Valley Fever") Am. J. Pub. Health **30:** 600-611 (June) 1940.

4. Gifford, M. A.: Coccidioidomycosis, Kern County, Annual Report of Kern County Health Department for the Fiscal Year July 1, 1938 to June 30, 1939, pp. 73-79.

5. Stewart, R. A., and Meyer, K. F.: Isolation of Coccidioides Immitis from the Soil, Proc. Soc. Exper. Biol. & Med. **29:** 937-938 (May) 1932.

6. A description of the roentgen findings on our students has been reported by R. A. Powers and D. J. Starks in Radiology **37:** 448-453 (Oct.) 1941, in an article entitled Acute (Primary) Coccidioidomycosis: Roentgen Findings in a Group "Epidemic."

was subsequently proved by cultures and animal inoculations.) Fluoroscopy and roentgenograms on May 27 revealed that a cavity had developed in one of the consolidated areas. Moreover precipitin and complement fixation tests on his serum were positive for coccidioidal infection.

After the diagnosis of active coccidioidal infection was established, blood was drawn for sedimentation and precipitin tests from the other members of the expedition who had symptoms. Specimens of sputum were collected from all who could furnish any. Coccidioidin tests were repeated on most of them.

On June 4 all 13 of the group who were still on the university campus (O. C. was in the Stanford University Hospital) were assembled. Histories were taken of the movements of each person while on the field trip results. Three others of the faculty group had positive coccidioidin reactions but negative precipitins, normal sedimentation rates and entirely normal blood pictures. One (Professor A.) had taught for some time years before in Rosedale near Bakersfield in the San Joaquin Valley, where Coccidioides is endemic. Professor W., also with a positive coccidioidin reaction, had taught near Bakersfield at McFarland. While he was in the San Joaquin Valley, he had a severe respiratory illness which was diagnosed tuberculosis and was sent to a sanatorium for several months. However, tubercle bacilli were never recovered from his sputum and his illness may well have been coccidioidal. Miss T., also with a positive coccidioidin test, had made many field trips in the San Joaquin Valley and in San Benito County. She recalled no respiratory or other "flulike" illness.

Clinical History of Students and Faculty Members Making Up Field Trip

					Symptoms									Coccidioides in Sputum		Coccidioidin Test, Days from Exposure		Serologic Tests (Precipitin and Complement Fixation)	Blood Changes			
Name	Sex	Present at Rattlesnake Hole	Previous Contact with Endemic Areas	Incubation Period	Cough	Pleurisy	Fever	Nightsweats	Malaise	Headache	Backache	Anorexia	Weakness	Days After Exposure	Result	Negative	Positive		Sedimentation Index (Cutler)	Maximal White Blood Cells	Maximal Eosinophils	Roentgenographic Changes
O. C.	♂	+	?	9	+	±	+	+	±	+	+	+	+	30 to 45	+	..	26	+	26	17,700	8%	+
A. S.	♀	+	0	10	+	+	+	+	+	+	+	+	+	42	+	Faint + 25	35	+	23	20,550	5%	+
W. G.	♂	+	0	13	+	("Tightness")	+	+	+	+	0	+	+	33	—	..	38	+	20.5	15,000	5%	±
B. M.	♀	+	0	14	+	("Tightness")	+	0	+	+	+	+	+	33	—	..	27	+	23	15,800	6%	+
R. R.	♀	+	0	9	+	+	+	+	+	+	+	+	+	33	+	..	33	+	14	11,700	10%	+
D. S.	♀	+	0	13	+	+	+	+	+	+	Neck	+	+	33	+	Faint + 27	38	+	23	11,000	8%	+
J. B.	♀	+	0	Not definite	±	0	0	0	0	0	0	0	0	43	—	..	33	+	13	12,200	6%	+
Miss T.	♀	+	+	0	0	0	0	0	0	0	0	0	0	33	—	..	39	—	2.5	8,400	2%	Fluoroscopy negative
Dr. W.	♂	+	+	0	0	0	0	0	0	0	0	0	0	33	—	..	39	—	1	6,400	2%	..
Prof. A.	♂	—	+	0	0	0	0	0	0	0	0	0	0	33	—	..	39	—	6	7,600	2%	..
J. G.	♀	—	0	0	0	0	0	0	0	0	0	0	0	33	—	34	0	—	6	8,500	1%	Slight accentuation of bronchovascular shadows at right base
H. W.	♂	—	0	0	0	0	0	0	0	0	0	0	0	33	—	39	0	—	2	4,100	2%	—
B. H.	♀	—	0	0	0	0	0	0	0	0	0	0	0	33	—	39	0	—	5	10,300	8%	Fluoroscopy showed heavy root markings; x-ray entirely normal
Mrs. F.	♀	—	?	0	0	0	0	0	0	0	0	0	0	33	—	39	0	—	6 (80')	10,650	No differential count	Fluoroscopy negative

and of any subsequent illnesses. Coccidioidin tests were performed on those who had not yet been tested, blood counts made, erythrocyte sedimentation rates determined and blood removed for precipitin tests. More sputum cultures were also obtained.

On the basis of the positive coccidioidin reactions, positive precipitin tests, rapid sedimentation rates, characteristic blood counts and densities in their roentgenograms, all 6 students who had been ill were judged to have had primary coccidioidal infections. Four of the group had Coccidioides immitis recovered from their sputums. One other student, J. B., felt well but had a positive reaction to 0.1 mg. of coccidioidin, a positive precipitin test, accelerated sedimentation rate and eosinophilia, bringing the total to 7 infections. The remaining 3 students had been well, gave negative coccidioidin reactions, had normal sedimentation rates and normal blood counts (one had 8 per cent eosinophils) and their serums did not show precipitins. One of the faculty group (Mrs. F.) similarly gave negative

One of the most interesting aspects of the epidemic was the suggestion as to where the fungus could have been inhaled. The nature of the epidemic suggested that the infected students must have had a common massive exposure which the 4 negative to coccidioidin did not experience. The 3 coccidioidin positive faculty members might or might not have been exposed, previous studies having indicated that one infection apparently results in an immunity.

The way the groups traveled in their automobiles precluded dust from the road as the cause, since uninfected students were in each auto load. At night the blankets were laid directly on the ground, but the infections were so scattered that no common exposure could have been possible. The manner in which the groups worked in their specimen hunting obviated any possibility of a suitable exposure except for one occasion: When the expedition was in the Panoche Valley on April 27 it stopped along a creek bank to collect flowers and explore an abandoned quicksilver mine. Some one

observed a rattlesnake which crawled down a ground squirrel hole. O. C. began digging industriously. Later he recalled the occasion because the dust was so dense and he was in the thickest of it. He was assisted or surrounded by all the other students who were infected, and also by Professor W. and Miss T., who, it has been shown, apparently had experienced a previous infection with Coccidioides. However, the 4 giving negative reactions to coccidioidin (Mrs. F. and 2 of the 3 students) were not anywhere near the digging, and the third student, W., was not close at hand either.

Thus circumstantial evidence strongly implicated the vicinity of the rattlesnake hole. In August 1940 one of the recovered students guided one of us back to the spot. Specimens of the soil were collected and from them Coccidioides immitis was recovered.

COMMENT

Not only is the mechanism of coccidioidal infection verified but also is resistance to exogenous reinfection substantiated. The incubation periods, nine to fourteen days, are likewise in accordance with the range previously established.[3] Among the cardinal symptoms and signs summarized in the accompanying table, the pain or "tightness" in the chest is the most useful in a differential diagnosis. It is to be noted that none of the patients had erythema nodosum or multiforme.

REPORT OF CASES

CASE 1.—O. C., a male graduate student aged 21, was born in San Francisco and lived there all his life except that from 1934 through 1936 he lived in San Mateo and since 1936 he has been at Stanford (Palo Alto), and also during some summer vacations. In the summer of 1938 he worked on an Associated Oil tanker on the Sacramento and San Joaquin rivers. He did not go inland farther than 2 miles. In the summer of 1939 he visited friends in Fresno on week ends. He has also made occasional visits around Tracy and a few trips through the San Joaquin Valley.

On May 6, 1940, nine days after returning to Stanford from his rattlesnake digging in San Benito County, he suddenly felt weak and feverish. However, he had no actual malaise and attempted to throw off the illness with a vigorous workout followed by a half mile swim. The following day, May 7, the fever persisted, his appetite left him and a severe backache developed which lasted until the next day. He also began to cough and the coughing continued for a month and a half. On this second day of illness, despite his feeling of weakness, he played football for two hours. On awakening May 8 he felt "jittery" and so weak that he could hardly climb out of bed. To the other symptoms was added a severe frontal headache; at last admitting he was ill, he consulted the Men's Health Service. When the patient's temperature was found to be 103 F. he was sent to the Palo Alto Hospital under the care of one of us (B. D.). That night he had a drenching nightsweat, and severe nightsweats persisted until the last week in June. The day after entry into the hospital severe "backache" recurred. The previous attack had been unaffected by breathing, but this time breathing and coughing exaggerated it, suggesting pleurisy. Suspicion having been aroused by "a few faint tinkles," a roentgenogram was obtained. It revealed multiple circumscribed areas of increased density. Sulfapyridine was given for five days. The temperature dropped but the development of nausea and a dermatitis necessitated the discontinuance of this therapy. When the fever recurred sulfanilamide was tried. The fever continued and the dermatitis returned, so the drug was stopped. Blood cultures, serologic tests, sputum examinations and cultures being persistently negative and coccidioidin tests being interpreted as equivocal, the patient was transferred to Stanford University Hospital in San Francisco on May 24. Sulfathiazole treatment was initiated (1 Gm. every four hours) but discontinued after three days and a total dosage of 47 Gm. because of increase in temperature (to 103.6 F.), malaise, generalized arthralgia and dermatitis. Meanwhile, on May 26 the coccidioidin test with 0.1 mg. of coccidioidin became positive (12 by 12 mm.). Coccidioides immitis was recovered from stomach washings made the same day and repeatedly from sputum specimens obtained over a period of two weeks, the last successful attempt being on a specimen obtained June 11, more than a month after onset of the illness. Precipitin and complement fixation tests for Coccidioides were also positive. Roentgenograms and fluoroscopy on May 27 revealed a cavity in one of the consolidated areas. However, the defect rapidly closed. The blood count on May 28 showed 16,100 white blood cells with 68 per cent polymorphonuclear neutrophils, of which 36 per cent were banded cells, 8 per cent eosinophils, 2 per cent basophils, 21 per cent lymphocytes and 1 per cent monocytes. There were 4.91 million erythrocytes and 13.72 Gm. hemoglobin (80 per cent Sahli). The erythrocyte sedimentation rate was 26 mm. in sixty minutes (Cutler). After the sulfathiazole was discontinued his only complaints were fever, nightsweats and cough. The cough gradually diminished during the early part of June and by June 21 had ceased entirely. At the same time nightsweats stopped and by the end of the month his temperature remained normal all day. He returned home July 3 but was kept in bed until August 1. Then, since he had continued afebrile and his sedimentation index was only 7.5 mm. in sixty minutes (Cutler), he was gradually allowed up. He was permitted to return to Stanford in the latter part of September and carried his full research load without ill effect. Regression of the pulmonary densities as revealed by roentgenograms continues, though slowly, and no cavities are discernible. His sedimentation rate is consistently 1 mm. in one hour (Cutler's method).

CASE 2.—A. S., a female sophomore student aged 20, born in Germany, moved to Wisconsin in 1927 and to California in 1934. She remained in the region around San Francisco Bay and her only contact with the San Joaquin Valley was on two trips en route to other parts of the state.

On May 7, 1940, ten days after participating in the rattlesnake digging, she reported to the Women's Health Service with a complaint of backache radiating to the right side of the chest, relieved by infra-red light treatment. On May 8 she had fever and nightsweats with some generalized aching. The third day, May 9, the backache and pain in the right side of the chest recurred with increased severity, and some discomfort was noted in the left side of the chest. These symptoms were accompanied by a nonproductive cough, anorexia and severe frontal headache. Taping reduced her discomfort slightly but infra-red treatment made it worse. Her temperature was 100.6 F. and she entered Palo Alto Hospital under the care of one of us (R. S.). There were no physical abnormalities, but roentgenograms of her chest on the day of entry revealed a rounded opacity in the parenchyma of the lung opposite the right hilus. The total white count was 20,550 with 86 per cent polymorphonuclear neutrophils, 9 per cent lymphocytes, 2 per cent monocytes, 3 per cent eosinophils (subsequently rising to 5 per cent; shown in table). The hemoglobin level was 80 per cent Sahli with 4,650,000 erythrocytes.

Sulfanilamide therapy was started the day of entry and 515 grains (34 Gm.) was given within the next ten days without appreciable effect. The pain in the chest cleared in two days but the anorexia, headache and dry cough persisted. On May 10 a rash resembling tinea corporis appeared on the buttocks but disappeared in two days after local application of tincture of iodine.

The temperature reached a maximum of 103 F. on May 10 and dropped thereafter. It persisted between 99 and 100 F. until June 1. On May 22 she was discharged from the hospital. Sputum cultures made while she was hospitalized yielded only a yeast. A coccidioidin skin test (0.1 mg.) was "faintly positive" on May 19. When repeated on May 29 the same test was strongly positive. Serologic tests on blood drawn June 1 and repeatedly thereafter indicated active coccidioidal infection. Although initial cultures were negative, Coccidioides immitis was recovered in the medical school public health laboratory by means of guinea pig inoculation of treated sputum collected June 6 and June 9. Anorexia persisted until June 1, and cough

and headaches lasted until June 18. Some weakness continued throughout the summer, but by September she felt quite well and had regained the 12 pounds (5.4 Kg.) that she had lost during her illness. Roentgenograms showed gradual clearing of the density. She remained well during the ensuing year.

CASE 3.—W. G., a male graduate student aged 24, was born in Ohio and lived there until he came to Stanford in October 1938. His only contact with the San Joaquin Valley was one trip along Highway 99 en route to Los Angeles.

On May 10, 1940, thirteen days after participating in the rattlesnake digging, he began to cough, lost his appetite, felt feverish and complained of a frontal headache and a sense of oppression in his chest without actual pain. A "tightness" in his chest remained for only thirty-six hours and malaise was mild and also transient. An occasional nonproductive cough persisted until June 13. The headache continued for only three days. Continued anorexia caused him to lose 6 pounds (2.7 Kg.). During the latter part of the first week of his illness nightsweats were so severe as to dampen his pajamas. The duration of the fever was unknown, but it must have been for at least one week. On May 20 he was called in by the Men's Health Service for a check-up which was being made of all members of the expedition. His temperature was found to be 100 F., so he was sent to the hospital for roentgen and laboratory examinations. The roentgenograms showed an increase in lung root density but no definite areas of infiltration. After three weeks of illness, he noted a considerable chilliness on arising but had no real chills at any time. There was no backache, sore throat or nervousness other than pruritus. Instead of having insomnia, he was tired and slept about sixteen hours a day for the first three days of the attack. On June 5 his appetite was well on the way back but was still not normal. Outside of occasional cough and extreme fatigue no other symptoms were present. A coccidioidin test with 0.1 mg. of coccidioidin on June 4 measured 30 by 30 mm. By the time he was asked to collect his sputum on May 30 scarcely any could be raised. Coccidioides immitis was not recovered. However, his sedimentation index of 20 mm. (Cutler) and his blood count were supporting evidence, as shown in the table. Serologic reactions of his blood, both positive complement fixation and heavy precipitins, were characteristic of primary coccidioidal infection. He rapidly regained his strength. By June 23 he felt fine and remained well during the ensuing year.

CASE 4.—B. M., a female senior student aged 22, was born in Washington and came to California as a Stanford freshman in October 1936. Her only contact with the San Joaquin Valley was on occasional trips to Yosemite and Los Angeles. Only once while on such a trip did she stop overnight in the valley.

On May 11, fourteen days after the rattlesnake excavating and while in Sacramento en route to Lake Tahoe, she had a sudden onset of chills, then felt hot and completely lost her appetite, all of which she attributed to the heat. These symptoms continued and when she reached Tahoe she was short of breath, a condition she attributed to the altitude. The following day she began to ache all over and had a severe frontal headache. The fever and anorexia continued, and in addition she had diarrhea, vomiting and vertigo. Returning to Stanford on May 13 with severe backache, a temperature of 102 F. and a cough, her condition was diagnosed as possible measles and she was sent to the Palo Alto Hospital. Physical examination was entirely negative except for the elevated temperature and a generalized ("somewhat urticarial" according to her attending physician) eruption on her legs and thighs, with a few lesions on her back. The lesions itched and were diagnosed hives. They lasted four to five days and recurred once again on May 25. The malaise became worse and she noted tightness throughout the chest. It was not actually pleurisy but it caused her to have shortness of breath. She remained in the hospital five days and then, with the cough diminished and fever ended, she was discharged. However, the malaise, insomnia, loss of appetite and headache continued, as did the nonproductive cough. Small blisters appeared on the palms of her hands May 17 and remained for three days, after which the skin peeled. The appetite began to return after two weeks, the weight loss having been at least 5 pounds (2.3 Kg.). Headaches stopped May 25. When interviewed June 5, she still had this sense of oppression in the chest, considerable dyspnea, periods of backache and a dry cough. She tired readily and did not have her customary energy. A coccidioidin test with 0.1 mg. of coccidioidin performed May 24 measured 50 by 90 mm. By the time she was asked to collect her sputum, May 30, scarcely any could be raised. Coccidioides immitis was not recovered. However, her sedimentation index of 23 mm. (Cutler) and her blood count were supporting evidence. Roentgenograms taken May 24 showed two areas of density beyond the left lung root and at the left base. These findings assume even more significance in view of the considerable clearing by June 12 and complete clearing by August. Serologic reactions of her blood, both positive complement fixation and heavy precipitins, were characteristic of primary coccidioidal infection.

The cough continued until June 12. When seen June 21 she stated that only in the last two or three days had her appetite been good. She still tired easily and became short of breath but otherwise felt all right, though not as full of "pep" as usual.

During the summer she was very quiet. Her roentgenograms cleared (as previously noted) and the lost weight was regained by August. By September 30 she felt fully recovered. She carried a heavy schedule during the year and felt entirely well.

CASE 5.—D. S., a female junior student aged 20, was born in San Mateo, Calif. She resided there two years, then went to Sacramento for nine years and lived continuously in Berkeley thereafter (nine years) until she started to Stanford in October 1937. She was in the San Joaquin Valley in 1937 en route to Death Valley and once took a field trip to Yosemite by way of Los Banos.

On May 10, 1940, thirteen days after the rattlesnake episode, she had an abrupt onset of pain in the neck and anterior part of the chest, cough, loss of appetite and generalized aching. She also felt feverish. The fever and aching persisted for three days and on the third (final) day she went to the Women's Health Service, where she was diagnosed as having myositis. The pleurisy was fairly severe, first on the right side and then beneath the breast bone, and remained for one week. It then disappeared and recurred twice, the last time being May 26. Both recurrences were for only a couple of days with generalized pain. The severe pain in the neck also lasted approximately one week. The cough, accentuating the pain in the chest, was persistent and produced little sputum. After three weeks it gradually abated and at the same time her appetite began to improve. No loss of weight was detected. The patient had severe nightsweats on the night of May 12 but noted them only on that occasion. Her headache, which began the day after onset of her condition, was located on the right side of the head and continued throughout the summer. The only cutaneous lesions that developed were hives, which appeared over the buttocks at the onset and which recurred June 4. These cutaneous lesions itched and were not at all like erythema nodosum.

A coccidioidin test (0.1 mg.) performed May 24 was equivocal. Repeated June 4, it was definitely positive (10 by 10 mm.). Coccidioides immitis was recovered at the medical school by culture of sputum collected May 30. Roentgenograms, taken on May 24, showed heavy lung root markings with density spreading into the right upper lobe. By June 12 there was considerable clearing of this density, and a roentgenogram taken October 9 showed complete clearing except for a suggestion of lung root enlargement on the right. Her serologic tests were also characteristic of primary coccidioidal infection.

During the forepart of the summer she improved rapidly, but in the latter part of August there were three nights in which there were nightsweats. She tired readily but by the latter part of September, when the university reopened, felt quite well, having gained 12 pounds (5.4 Kg.). However, during the autumn quarter she studied hard and found that she lacked her former strength. She lost 22 pounds (10 Kg.) during this period. She had a mild attack of "flu" in December with a normal recovery. A year after her illness she felt entirely well.

CASE 6.—R. R., a female sophomore student aged 19, was born in Oklahoma. She never lived in Texas or Arizona but once stayed two weeks in Santa Fe, N. M. She first came to California when she entered Stanford in September 1939. At no time had she been in the San Joaquin Valley.

On May 6, 1940, nine days after witnessing the rattlesnake digging, the patient felt feverish, ached all over, had a severe headache and backache, pain in the left side of her neck and left side of the chest, completely lost her appetite, was nauseated and vomited three times. That night she had the first of a month long series of nightsweats. The symptoms did not abate but grew worse, and after two days (May 8) the pain in the back and chest was so severe that she reported to the Women's Health Service. Physical examination failed to disclose any positive conditions. She had been swimming the day prior to the onset and her condition was diagnosed as strained muscles from diving. She was given heat treatment and was taped. The taping partially relieved the chest pain, which was accentuated by breathing, but the heat only increased the discomfort. A slight nonproductive cough which began on May 7 became much more severe on May 11, but its persistence was matched by the scantiness of the sputum. A small cutaneous lesion which appeared on her chin May 9 was diagnosed as either impetigo or poison oak and cleared after nine days. Insomnia was another feature of the illness. After eight or nine days the pleurisy and backache diminished but the other symptoms persisted for three weeks during which time the patient lost 9 pounds (4.1 Kg.). On June 1 she still had an evening temperature of 100 F., but it then abated along with her malaise and anorexia. The cough and headaches persisted for another week.

On May 30, 0.1 mg. of coccidioidin intracutaneously produced a reaction measuring 60 by 80 mm. with vesiculation of 10 by 10 mm. From sputum obtained May 30 and examined at the medical school, Coccidioides immitis was recovered both by cultures and by animal inoculation. Roentgenograms taken May 27 showed an area of patchy density near the periphery in the right costophrenic angle and a similar area of homogeneous density under the second right anterior interspace. These densities had cleared only slightly by October 9. The accelerated sedimentation index (14 mm. Cutler) and 10 per cent eosinophils were typical conditions and the serologic reaction was characteristic of primary coccidioidal infection.

She was exhausted by slight exertion until the middle of June (five weeks after the onset). During the forepart of the summer her strength gradually returned, but in the middle of August she began coughing and the left base of her chest hurt for six days. Then the pain gradually departed and by the middle of September she felt fairly well except for frequent headaches. In the autumn quarter she grew steadily more tired and her geology field trips exhausted her. In December she had an attack of influenza and during the rest of the school year continued to feel below par. However, her sedimentation index remained normal (under 5 mm. Cutler) and her precipitin and complement fixation tests for Coccidioides became negative and remained so, indicating that the infection was quiescent.

CASE 7.—J. B., a female senior student aged 21, was born in Huntington Park, Calif. She had lived there all her life with the exception of four school terms at Stanford beginning in October 1936. There was no history of residence in the San Joaquin Valley but of occasional trips through the valley on Highway 99. Usually she traveled along the coast on Highway 101.

There was no illness after the return from the field trip except a slight cough with an indefinite date of onset (around May 20) and subsequent to a hayride. After the onset of the cough, she also had headache. However, there was not present loss of appetite or of weight, or generalized aching, fever, pleurisy, nervousness or insomnia. During the entire spring quarter she did not feel her customary "pep," but there had been no significant drop after the San Benito County trip.

A coccidioidin test (0.1 mg.) performed May 30, 1940 was strongly positive, measuring 60 by 80 mm. Although her slight cough was nonproductive, sputum was collected June 9 and June 14, but Coccidioides immitis was not recovered. A roentgenogram taken May 27, however, showed a peribronchial density at the right base, which had disappeared by August 21. Moreover, an accelerated sedimentation index (13 mm. Cutler) and 6 per cent eosinophils were additional corroboration of coccidioidomycosis. Finally, her serologic reaction was characteristic of primary coccidioidal infection.

SUMMARY

Seven out of 14 university students and faculty members were infected with Coccidioides immitis on a field trip to a region adjacent to the San Joaquin Valley. All 7 and 2 of the others who apparently had been immunized by previous infection were subjected to a heavy dust exposure. The fungus was recovered from the soil which had been the source of the dust.

The infections of 6 of the 7 victims were accompanied by moderately severe symptoms which lasted from three to six weeks, but all patients recovered without the development of coccidioidal granuloma.

A SURVEY OF COCCIDIOIDOMYCOSIS AT CAMP ROBERTS, CALIFORNIA

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In the early months of the development of Camp Roberts, among the many cases of acute respiratory illness receiving treatment at the Station Hospital, 2 cases of primary coccidioidomycosis were discovered. Camp Roberts lies on the western slope of the Coast Range Mountains of California, separated from the San Joaquin Valley by that range, and since this area had not previously been known to harbor the disease as an endemic focus a survey was undertaken to determine the extent of the disease locally, the results of which survey constitute the body of this report.

INTRODUCTION AND HISTORICAL DATA

Dr. Emmet Rixford of San Francisco reported in 1894 [1] a case of malignant ulcer of the skin caused by an agent which he and Gilchrist [2] named Coccidioides. This was the first report of this disease entity in the American literature, though the same disease had apparently been described in 1892 by Posada in Argentina. The infecting agent was a tiny spherule which multiplied by endosporulation and was capable of producing an ulcer if rubbed into the abraded skin of a dog; it was named Coccidioides because of its resemblance to Coccidia of animals. At first thought to be a protozoan, it was reported in 1900 by Ophüls and Moffitt [3] to be a fungus, readily cultured on various mediums. The disease coccidioidal granuloma proved to be a serious disorder, involving not only the skin but also many of the other viscera and leading to a fatal outcome in 50 per cent of the cases.[4]

By 1936 450 cases of coccidioidal granuloma had been reported in California, constituting the majority of all the cases on this continent. A striking feature was that most of the patients had lived a longer or shorter period of their lives in the San Joaquin Valley of California. The disease had been discovered in animals, as well as

1. Rixford, Emmet: A Case of Protozoic Dermatitis, Occidental M. Times **8**: 704-707 (Dec.) 1894.
2. Rixford, Emmet, and Gilchrist, T. C.: Two Cases of Protozoan (Coccidioidal) Infection of the Skin and Other Organs, Johns Hopkins Hosp. Rep. **1**: 209-268, 1896.
3. Ophüls, Wilhelm, and Moffitt, H. C.: A New Pathogenic Mold, Philadelphia M. J. **5**: 1471-1472 (June 30) 1900.
4. Beck, M. D.: Coccidioidal Granuloma, California State Department of Public Health Bulletin 57, June 1931.

in man, and pathologic investigation showed that the probable port of entry in most cases was the respiratory tract, with involvement of tracheobronchial and mediastinal lymph nodes, much the same as in tuberculosis. In fact, the mimicry of tuberculosis was striking in all phases and progress of the disease.

An important further step in the understanding of the infection was made by Gifford [5] and Dickson [6] during the period 1936-1937, when they proved that Coccidioides was the cause of a syndrome known colloquially in the San Joaquin Valley of California as "Valley fever" or "San Joaquin fever." This syndrome, previously well known but not understood, was characterized by the development of erythema nodosum and attendant systemic symptoms much like those of influenza. Coccidioides was cultured from the sputum of many patients and all were found to react positively to a cutaneous test with coccidioidin, a substance closely analogous to tuberculin. It was determined that "valley fever" was associated with the initial infection with Coccidioides and is the analogue of "childhood" tuberculosis. The name "primary coccidioidomycosis" was given to this symptom complex by Dickson.

Since then it has become clear that a majority of the residents of the San Joaquin Valley eventually become infected (70 to 80 per cent give positive reactions to the coccidioidin skin test after ten years' residence); that 2 to 5 per cent of those infected have the erythema nodosum syndrome known as valley fever,[7] whereas the remaining 95 to 98 per cent may be entirely asymptomatic but generally have respiratory symptoms frequently confused with influenza; that the granuloma or secondary stage (like "adult" tuberculosis) is, fortunately, quite rare, and that the San Joaquin Valley is not the only endemic focus but shares its stigma with parts of Arizona and Texas. Argentina and possibly even Italy and other continental areas had been implicated previously. Exactly what percentage of those exposed develop skin sensitivity to coccidioidin or manifest the symptoms of primary coccidioidomycosis is not known. Nor is there any exact information as to the reservoir from which the fungus comes to enter the human being, but it is presumed from the high correlation of frequency of new cases with dryness of the atmosphere that the soil harbors the fungus and gives it up as dust that may be inhaled. There is no information as to what percentage of those infected eventually have the dread granuloma, but its infrequency can be seen by the fact that while a large percentage of the population of the San Joaquin Valley (estimated population 750,000) is apparently infected with Coccidioides (sensitive to the coccidioidin skin test), the Department of Public Health of the State of California [8] reports an average annual incidence of only 46 new cases of coccidioidal granuloma. Susceptibility to the development of the granuloma is relatively high among the dark skinned races, and it is of note that cases of the granuloma show a much lower degree of skin sensitivity to coccidioidin than do those who have recovered from the initial infection without apparent residual disease.

5. Gifford, M. A.: San Joaquin Fever, Annual Report of Kern County Health Department for the Fiscal Year July 1, 1935 to June 30, 1936, pp. 22-23.

6. Dickson, E. C.: Valley Fever, California & West. Med. **47**: 151-155 (Sept.) 1937. Dickson, E. C., and Gifford, Myrine Ada: Coccidioides Infection (Coccidioidomycosis), Arch. Int. Med. **62**: 853-871 (Nov.) 1938. Dickson, E. C.: Primary Coccidioidomycosis, Am. Rev. Tuberc. **38**: 722-729 (Dec.) 1938; Coccidioidomycosis, J. A. M. A. **111**: 1362-1364 (Oct. 8) 1938.

7. Smith, C. E.: Epidemiology of Acute Coccidioidomycosis with Erythema Nodosum, Am. J. Pub. Health **30**: 600-611 (June) 1940.

8. Report of Bureau of Epidemiology, Department of Public Health, State of California.

MATERIAL AND TECHNIC

This report is based chiefly on the results of two skin test surveys made three months apart, the two surveys being made on the same group of persons, with a view to finding in how many instances the test became positive during the three month interval. In addition, there are reports of 3 cases discovered in the hospital—not a part of the survey.

Coccidioidin supplied by Dr. C. E. Smith of Stanford University School of Medicine was diluted with saline solution to a concentration of 1:1,000. While it is conceivable that 1:100 dilution would show sensitivity occasionally where 1:1,000 would give a negative or questionable response, it has been found that for practical purposes 1:1,000 is sufficient. The same bottle of undiluted coccidioidin was used as the source in the two series of tests, being kept during the interval in a refrigerator.

It cannot be said that a precisely constant amount of the antigen was injected in each patient. The necessity of doing the procedure with minimum delay required a special "mass attack" technic, and the amount of fluid lost in the hub of the needle and in expelling air bubbles prevented accurate measurement. The amount injected was determined by gross inspection of the wheal produced and averaged 0.05 cc. In no case was it more than 0.10 cc. nor less than 0.03 cc. It is my observation that the variation in amount, within the limits mentioned, is not significant except perhaps in distinguishing slight variations in the grade of the reaction. In other words, the positive reactors will appear in response to 0.03 cc. as surely as to 0.10 cc. but may be graded "one plus" with the former and "two plus" with the latter.

TABLE 1.—*Results of Coccidioidin Skin Tests*

	Number
First test, June 21, 1941	
Men tested	888
Positive	11
Second test, Sept. 13, 1941	
Men tested (less positives from first test)	736
New positives	14

The two series of tests were made on a battalion of men plus a few men from three other battalions newly arrived at Camp Roberts. The first test series was done June 21 on a battalion of troops that had arrived between June 12 and June 15. The troops were gathered from the Middle West—Illinois, Missouri, Nebraska, Arkansas and Texas—and no attempt was made to list them by residence except for those who reacted positively to the first test.

The second series of tests was made on the same men on September 13 after three months of training in and about Camp Roberts and just before their transfer to other camps.

All reactions were read at from forty-four to forty-eight hours and were recorded thus:

± definite induration and erythema but less than 1 cm. in diameter.

+ induration of 1 cm. in diameter.

++ induration of 1 cm. in diameter plus flare of erythema of 1 cm. or more.

+++ induration of 2 cm. or more.

++++ vesiculation.

Those reacting positively to the second test who were previously demonstrated to be nonreactors were questioned regarding symptoms during the three month

interval, and roentgenograms of the chest were made. All were carefully questioned regarding visits to other localities during this time.

In some cases, specimens of the blood were sent to the Department of Public Health and Preventive Medicine of the Stanford University School of Medicine in San Francisco for serologic tests. Under the supervision of Dr. C. E. Smith the specimens were examined for the presence of precipitins and for complement fixation according to technics described elsewhere. In 1 case, sputum was forwarded to Smith for culture and animal inoculation, since the final determination of the nature of the fungus depends on its ability to produce the typical reaction in animals.

The author wishes to express appreciation for the invaluable aid given by Dr. Smith and also by Lieut. Col. William Levin of the Sanitary Corps, Lieut. Col. Warfield W. Lewis of the infantry, Private Dernbach and others. Each of these rendered service without which this work would have been entirely impossible of achievement.

RESULTS OF SURVEY

The first series of tests was accomplished on 888 men. Eleven were found to give a positive reaction, though they had been at Camp Roberts too short a time to have picked up the disease here (tables 1 and 2). Of these positive reactors, 1 had lived only in Montana and Idaho, 1 had lived only in Arkansas not far from Texas, 6 had lived in Texas and 3 had lived in the San Joaquin Valley of California. Texas and California are already well recognized endemic foci of the disease, and the reaction in the first case suggests the possibility that Montana or Idaho may harbor the disease.

The second series included only 736 of the 877 who gave a negative reaction to the first test, because many of the men were not available, being on leave or having been transferred. Actually, of the 11 found positive in the first test, 8 were retested and all reacted positively the second time. Of the 736 men in the second series, all negative to the first test, 14 gave positive reactions. In other words, 14 men proved to be nonreactors in June reacted positively in September. Three of these had visited in the San Joaquin Valley during their stay at Camp Roberts, 7 had been to Los Angeles or San Francisco and 4 had not left the vicinity of Camp Roberts more than a few miles, having gone to Salinas (1 case), Pismo Beach (1 case) and Paso Robles (2 cases) (table 3).

TABLE 2.—*Previous Residence of Men Found Positive to Coccidioidin on Arrival at Camp Roberts*

Case	Reaction	Past Residence in Known Endemic Areas
C. M.	+	Bakersfield (San Joaquin Valley).
S. D.	++	Fresno (San Joaquin Valley)
R. S.	++++	Exeter (San Joaquin Valley)
I. C.	++	Texas
J. N.	+++	Texas
L. G.	±	Texas
R. R.	+++	Texas
R. M.	+	Texas
K. C.	±	Texas
J. R.	++	Arkansas only
C. B.	++	Idaho and Montana only

Of the 14 positive reactors, only 1, according to a check in the hospital records and answers to a questionnaire, had entered the hospital for any febrile or respiratory illness, though hospitalization is the routine procedure for any illness severe enough to prevent exercise of full duty. It is obvious that the onset of the infection was not attended by the development of distressing symptoms in most of the cases.

All but 4 of the 14 felt that they had at one time or another during the three months had a bad cold or influenza, and 3 had noticed a cutaneous eruption—nonitching red spots that looked like the positive reactions to the skin test. None of these eruptions had been examined by medical officers, so their description had to be a yes or no response to a questionnaire which was sent to all positive reactors (see table 4).

TABLE 3.—*Trips to Other Localities Made by Men Developing Positive Reaction While at Camp Roberts*

	No. of Cases
Visit to San Joaquin Valley	3
Visit to Los Angeles	4
Visit to San Francisco	3
No farther than Salinas (78 miles north)	1
No farther than Pismo Beach (50 miles south)	1
No farther than Paso Robles (15 miles south)	1
No farther than San Miguel (3 miles south)	1

Roentgenograms of the chest made September 16 on the 14 new reactors showed 1 case of pulmonary infiltration, a small area of light, uniform density much like the pulmonary manifestations in "childhood tuberculosis," and 2 cases with moderate enlargement of hilar lymph nodes. Check-up films of the 14 cases found on survey have not yet been made, and the results will be reported later.

REPORT OF CASES

Although many patients with primary coccidioidomycosis are entirely asymptomatic and must be searched out with the aid of a skin test survey, a few are ill, with symptoms like influenza or a bad chest cold. It was one such typical case that called our attention to the presence of Coccidioides in this location. The clinical summary is presented herewith:

CASE 1.—H. D. S., a white man aged 23, entered the hospital April 29, 1941 complaining of a cold and cough for three days, headache for two days and chills and fever for one day. Except for a temperature of 38.2 C. (100.8 F.), there was no abnormality apparent. The second day, the temperature went to 39.2 C. (102.6 F.) and the cough was worse, but three days later the fever was gone, the patient felt well and he was returned to duty. Five days later, May 8, he reentered the hospital because of pain in the right side of the chest of three days' duration and persistence of the cough. The temperature was 37.9 C. (100.2 F.) and there were rales at the right apex. The fever, cough and chest pain subsided a little but were still present after five days, at which time the white blood cell count was 12,300, with 50 per cent neutrophils, 32 per cent lymphocytes and monocytes, 12 per cent eosinophils, and 6 per cent basophils. The possibility of the trouble being tuberculous was considered and a roentgenogram of the chest was made, showing a fanlike area of increased density extending from the hilus to the right apex. In order to clarify the situation, a skin test with tuberculin was made and a coccidioidin test was done at the same time. After forty-eight hours, the tuberculin test was negative, and there was a definitely positive reaction to the coccidioidin (1 cm. by 1.5 cm. induration and erythema). The most startling development was the appearance at this time of erythema nodosum, a crop of red indurated spots on the legs, which had actually started two days previously and subsided gradually in a period of five days. The blood count was repeated, showing 10 per cent eosinophils, and a specimen of blood drawn June 7 was sent to Dr. C. E. Smith, who reported strong reactions to precipitin and complement fixation tests, "findings characteristic of moderately severe primary infection due to Coccidioides immitis." Clinically there was gradual improvement, a roentgenogram on June 6 showed almost complete resolution of the lesion previ-

ously noted and after a month of hospitalization and symptomatic therapy the patient was again returned to duty. No sputum culture was made. This man had lived in Nebraska prior to induction into the Army and had not been more than a few miles away from camp after his arrival here.

Another summary is presented to illustrate the severity of the symptoms in an occasional case and the difficulty in arriving at the proper diagnosis:

CASE 2.—E. R., a white man aged 24, entered the hospital Sept. 2, 1941 because of severe pain in the back which had appeared suddenly two hours previously while the patient was sitting at a table. For a few minutes he could hardly move, the pain was so severe, and he lost no time in getting to the hospital by taxicab. The pain was located in the lumbar region and was aggravated by respiratory movement or bending of the trunk. On entry there was evident pain and guarding of the muscles of the back, with impairment of the movements of respiration and bending of the trunk. There was no fever, the pulse rate was 88 and the blood pressure was 124 systolic and 80 diastolic. He was given sedatives and the clinical impression was that he suffered from an acute myositis secondary to chronic prostatitis. On the fourth day the temperature rose to 37.8 C. (100 F.), though the pain in the back had practically disappeared. Two days later the temperature was 38.3 C. (101 F.) and consultation was requested. In the next five days the temperature went gradually up to 40.7 C. (105.2 F.), with no symptoms except those of fever, and the patient was seen by eight different physicians, with diagnoses of pleurisy, pulmonary tuberculosis, pulmonary infarct, prostatitis, perforating ulcer of the duodenum, dissecting aneurysm, renal stone, bronchopneumonia, malaria, mediastinitis, undulant fever, typhoid, pyelitis and perinephric abscess. During this time he underwent lumbar puncture (the spinal fluid was normal) and catheterization (the urine was sterile); he was examined roentgenographically four times (no abnormal findings) and the following laboratory procedures were done: an electrocardiogram was made, a culture of the urine was taken, six routine urinalyses were made, six routine blood counts were made, the sputum was examined, a blood smear was examined for malaria, agglutination tests were done for evidence of undulant fever and for the typhoid-paratyphoid group and a stool culture was made. The red blood cells numbered 4,000,000 to 4,500,000 per cubic millimeter, the white blood cells 6,600 to 11,200 with from 56 to 80 per cent polymorphonuclear neutrophils and as much as 16 per cent eosinophils. All other tests were negative. On September 15, two weeks after entry, the clinical impression was that the disease was most likely tuberculosis of the pleura and hilar lymph nodes but possibly coccidioidomycosis, and a coccidioidin skin test was done. The response was brisk and violent, with vesiculation of the skin. Blood was drawn and sputum was collected for examination at Stanford, with a report of unusually strong and rapid precipitin reaction and positive complement fixation in the serum "characteristic of active coccidioidomycosis being well handled." From the sputum viable Coccidioides immitis was recovered, proved by culture and animal inoculation. The patient made a complete symptomatic recovery and was discharged from the hospital three weeks after entry. It is noteworthy that he did not manifest erythema nodosum at any time. He had spent all his life in Alabama, had never been out of the state prior to induction into the Army and since coming to Camp Roberts had made one trip to San Francisco, none to the San Joaquin Valley.

TABLE 4.—*Responses of "New Positive Reactors" to Questionnaire*

Case	Reaction of Second Skin Test	Hospitalized While at Camp Roberts	Bad Cold While at Camp Roberts	Red Skin Eruption Like Test	Results of Chest Roentgenograms Made Sept. 16, 1941
S. R.	±	No	Yes	Yes	Normal
J. F.	+	Yes	Yes	No	Normal
J. H.	++	Yes	Yes	No	Normal
W. J.	++	No	Yes	Yes	Hilar enlargement
H. K.	+	No	No	No	Hilar enlargement
W. M.	±	No	Yes	No	Normal
G. H.	++	No	Yes	No	Normal
J. M.	++	Yes	Yes	No	Normal
H. N.	±	No	No	No	Normal
I. W.	±	No	Yes	No	Normal
D. W.	±	No	No	Yes	Normal
W. W.	±	No	Yes	No	Normal
H. E.	++++	No	No	No	Pulmonary infiltration
F. L.	+	No	Yes	No	Normal

One patient was seen in the hospital as presenting a dermatologic problem:

CASE 3.—E. O., a white man aged 22, entered the hospital May 26, 1941 because of red spots on his legs of two days' duration. The eruption was somewhat tender and caused his legs to feel swollen. He had been in the hospital two weeks previously for pain in the chest, aggravated by breathing deeply, associated with a fever of 38.3 C. (101 F.), and had been released after one week, at which time he was afebrile and asymptomatic. The cutaneous lesion was typical erythema nodosum and the probability that it was a manifestation of coccidioidomycosis was considered. A roentgenogram of the chest showed a small patch of infiltration in the base of the right lung, and there was eosinophilia (18 per cent). The eosinophils two days later were recorded as 13 per cent. A coccidioidin skin test with the usual 1:1,000 dilution gave a very weak response, and the test was repeated with 1:100 dilution, giving a strongly positive reaction. This weak response to the coccidioidin is very unusual, since patients with erythema nodosum are notorious in the vigor of the sensitivity of their skin. Serologic reactions on the patient's blood, done by Dr. Smith, were strongly positive.

The erythema nodosum cleared in ten days, leaving only a brownish discoloration. The chest symptoms were of no concern, and the patient returned to duty. He had lived in Minnesota all his life prior to coming to Camp Roberts and after his arrival here had been no farther away than San Luis Obispo.

COMMENT

The chief significance of the investigation here reported is the demonstration of the fact that coccidioidomycosis can be acquired in the environs of Camp Roberts, California, a hitherto unknown endemic focus. This fact has been proved by the finding of 14 persons who were known to have given negative reactions to the coccidioidin skin test on arrival here and positive reactions three months later. It might be said in criticism of this statement that (1) the positive skin test is not specific but may have developed in response to some factor other than the exposure to Coccidioides, (2) the proved exposure may have taken place before arrival at camp, as while traveling across the country, (3) the proved exposure may have been acquired after arrival here but while visiting in some nearby area such as the San Joaquin Valley. In refutation of these criticisms it must be pointed out (1) that the skin test has apparently been proved to be quite specific, as determined by its use over a period of years, (2) that, while it must be admitted that some of the men may have been exposed to the disease en route to Camp Roberts the possibility of this is slight and (3) that careful questioning regarding trips to other localities after arrival here demonstrates that in at least some of the cases the exposure must have been here. Three of the 14 had visited in the San Joaquin Valley, 7 had been to Los Angeles or San Francisco but had not been in the San Joaquin Valley and 4 had not left the vicinity of Camp Roberts more than a few miles, the actual far points being Salinas, Pismo Beach, Paso Robles and San Miguel.

By extrapolation, if it is assumed that the percentage of men found infected is uniform throughout the camp, it could be estimated that, of the 20,000 to 25,000 men here, from 400 to 500 acquired primary coccidioido-

mycosis between June and September of this year. Observations elsewhere indicate that the incidence of new cases is highest in the dry months, falling to almost nothing in the wet winter months, so that the number of cases developing in three months of the summer represents nearly half of the annual incidence.

One feature of interest is the sporadic nature of the infection. The men tested in the two series were grouped almost equally into four companies, but the new positives were all in two of the companies, the other two companies being entirely free of new cases. Three of the new positives were White, Whitfield and Wilson, alphabetically contiguous on the company roster and presumably together on many bivouacs and maneuvers. It is possible that all were infected by the same gust of wind, carrying dust from a particularly heavy growth of the fungus.

Of the 14 men with proved new coccidioidomycosis, only 1 had entered the hospital for a respiratory or febrile illness. Two others had been hospitalized, one for a head injury and one for flat feet. There is no provision at Camp Roberts for resting off duty. If a soldier is not feeling fit for strenuous duty he enters the hospital. It is therefore obvious that the morbidity associated with the onset of coccidioidomycosis is almost insignificant in most cases. Some of the patients, however, suffered illness sufficient to incapacitate for military duty. In fact, the discovery of the presence of coccidioidomycosis at Camp Roberts depended on the typical symptoms occurring in one of the early patients.

When symptoms do occur in association with the onset of the disease, they may be of great diversity. Apparently there may be any combination of the various "typical" stigmas, and any grade of severity may exist. The symptoms considered characteristic include malaise, weakness, fever, chills, chest pain, cough and dyspnea, and the common manifestations include erythema nodosum, erythema multiforme, pulmonary rales, roentgen evidence of pulmonary or mediastinal lymph node disease and eosinophilia. Of course, a positive coccidioidin skin test may be presumed to exist in all new cases after the first five to fifteen days. The presence of a positive skin test, however, does not necessarily indicate a recent or active stage of the disease.[7] Like the reaction to tuberculin, the skin test is positive for many years after the primary infection, presumably for life. Serologic evidence of the disease, in the nature of a precipitin reaction or a complement fixation, is present in the vast majority of cases; at least, in all our cases in which the tests were made they were found positive. The sputum yields the fungus itself in approximately 50 per cent of cases of erythema nodosum of coccidioidal etiology, according to other investigators.[7] Detection of the fungus requires culture of the sputum and inoculation of guinea pigs or mice with any suspicious growth, because direct microscopic examination of sputum or colonies from primary culture does not provide any sure differentiation from other fungi. While the final proof of the diagnosis depends, of course, on the recovery of the etiologic agent, for practical purposes diagnostic error is minimal if the skin test, eosinophilia, pulmonary signs and symptoms and skin manifestations are typical.

SUMMARY

1. Several cases of primary coccidioidomycosis developed in the vicinity of Camp Roberts, California, a hitherto unknown endemic focus of the disease.

2. Of 736 soldiers who came from other parts of the United States to Camp Roberts, 14 became infected during three months' residence here, from June to September.

3. The morbidity associated with the onset of infection is almost negligible in most cases.

4. Rarely a patient becomes quite ill at the onset of the disease, with more or less fever, cough, pain, cutaneous eruption and pulmonary infiltration.

OBSTETRICS IN WARTIME

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On Sunday morning Dec. 7, 1941, out of literally a clear sky, Honolulu and its environs suddenly suffered a severe bombing. The details of the damage done, the number of civilian and military casualties and the military aspects of the problem are not the purpose or province of this paper. The sudden violence of this catastrophe did awaken the world to the possibility that a similar event might happen almost anywhere else.

Much will be written and much will be said regarding the care of casuals, emergency aid stations, police and fire protection and a number of other phases of community activity under similar circumstances; the specific problem of this paper is to consider obstetric management under crisis conditions. It is probable that this problem is just as real as the aforementioned problems; it is also probable that this problem as it existed in Honolulu would be paralleled in any other community. The experiences of this community are therefore delineated here in the hopes that they may be of help and guidance to other communities in making plans for war time conditions or a possible sudden catastrophe.

PEACE TIME SETUP

Hawaii is a group of islands and therefore a scattered community with problems of transportation much greater than in most mainland communities. Honolulu is the only metropolitan area with a population of 200,000; the rest can be accepted as essentially rural with highly organized plantations making up the bulk of the latter. The 400,000 odd population gives birth to about 10,000 babies yearly; this is a very mixed population, nearly half being Orientals. Oahu is not the largest island, but it contains the bulk of the population and nearly all the military activities, personnel and defense equipment; it was this island which was the target for the Japanese attack.

Numerous factors contributed to a very poor obstetric record in this community until about a decade ago. At that time the outstanding facts showed, briefly, that:

Almost 50 per cent of deliveries were unattended.

Only 25 per cent were hospital deliveries.

Less than one third of deliveries were by physicians.

Maternal mortality rates ranged around 9 per thousand live births.

Infant death rates were around 90; they had previously been consistently over 200 in some communities.

Nobody had any control over midwives, and there was no one to question their qualifications or abilities.

There was no regulation of hospitals accepting maternity cases.

Almost every physician was doing some obstetrics, and there was no one to question his methods or end results.

Antepartum care was the exception rather than the rule.

The advent of a maternal and child health program under the board of health proved very useful as a state agency in effecting improvements, and about it could be built a sane and practical program of maternal welfare. With an obstetrician and a pediatrician at the head of such a bureau, many accomplishments were recorded which tended materially to change the obstetric complexion. In contrast with the conditions of ten years ago, the following briefly shows the present status:

About 80 per cent of deliveries occur in hospitals.

More than 80 per cent of deliveries are attended by a physician.

The maternal mortality rate is 1.9 per thousand.

The infant death rate is around 40.

Less than 10 per cent of deliveries are unattended.

Midwives are under strict control by the board of health; there are fewer midwives, and midwife deliveries are decreasing in number.

There are forty antepartum clinics, carefully supervised, offering services even to remote communities.

Antepartum care is the rule rather than the exception.

An educational program has taught the expectant mother to demand hospital deliveries by a physician.

All hospitals accepting maternity cases are inspected yearly. They have been compelled to come up to minimum standards of equipment and service (separate nurseries, incubators, delivery rooms, isolation facilities, 75 square feet per adult bed, and so on).

Obstetric consultation services are offered by qualified obstetricians.

Each maternal death is carefully investigated.

Refresher courses in obstetrics and other teaching methods have awakened the general practitioner to his responsibilities in his obstetric practices, with noticeable improvement.

With this record of achievement, it is logical that the state agency should be in a key position to make plans for a major disaster and to help execute such plans when catastrophe arrives. Any community now making similar plans might do well to consult its own state agency, because it is in the best position to have a broad perspective of the community problems.

DISASTER PLANS

Honolulu had realized its precarious position and had probably gone further in perfecting major disaster plans than most similar mainland communities. With "M-Day" funds set up through legislation and headed by a major disaster council, months of planning and training found Honolulu with plans which came in handy when catastrophe overtook us suddenly. Of all the civilian groups, the medical fraternity was probably best prepared. This is proved by the facts that within about an hour's time after bombing began the following medical activities were in evidence:

First aid stations, completely staffed with doctors, nurses and litter bearers, were at their stations and functioning throughout the city; although the equipment was inadequate at first, the personnel were adequately trained in their duties by many weeks of first aid instruction.

Civilian surgeons with previous instruction in military surgery were immediately available for civilian hospitals and the surplus of doctors was rushed to a military hospital, where they proved useful in caring for a large number of casuals. (The physicians had previously been carefully catalogued regarding their special abilities, training and whereabouts.)

By previous arrangement, many station wagons and light trucks were immediately available for ambulance service. A corps of trained women drivers proved very useful.

Equipment for producing plasma and a plasma bank of about two hundred flasks were available through previous foresight and proved most useful. The equipment was immediately put to further use and the plasma bank has now been built up to about five thousand flasks.

Civilian hospitals were immediately expanded to maximum capacity by adding stored equipment and by evacuating the less ill patients to their homes. The precision with which civilian hospitals functioned was the reward of careful planning and previously trained personnel.

The board of health immediately went on a twenty-four hour basis to lend every effort in safeguarding the health of the community.

While a sudden disaster instinctively turns one's mind to the importance of first aid, of immediate care of casuals, of ambulances and trained personnel to care for the wounded, it is also well to keep in mind that, war or no war, women will keep right on having babies and they must also receive adequate care. What is more, the experiences in London showed that, under the acute stress of a bombing, women are apt to go into premature labor or to abort. Plans for a major disaster must therefore include obstetric provisions.

Locally our plans had been directed along several practical lines and, fortunately, had had some time to mature before the crisis hit us. The following proved to be very workable:

1. Obstetricians were assigned to maternity hospital posts instead of being used in other hospitals to care for casualties.

2. Pediatrician-public health nurse teams, equipped with incubator, oxygen and other equipment, were available for premature infants born before getting into a hospital.

3. A careful survey of all available maternity bed facilities in the community had been made and had proved the fact that such facilities were already overtaxed; there had been a rapid increase of population as the result of importation of defense workers and increasing military personnel. The sudden crisis caught us before we had been able to expand our maternity facilities, and it became obvious that to increase the obstetric load was possible only by decreasing the stay post partum. Our patients were therefore forewarned that, in case of a disaster, we would continue to offer the facilities of our delivery rooms but would expect them to return to their families earlier than under normal conditions.

4. Arrangements were made with the hospitals to prevent the encroachment on the maternity departments by casuals.

5. All public health nurses were given a refresher course in practical obstetrics to improve their efficiency in home deliveries.

6. Home delivery packs were made up and kept in readiness in a convenient place for district nurses or doctors.

7. Nursing personnel in obstetric departments should be kept intact regardless of the extra load the rest of the hospital might suddenly be compelled to carry.

8. All expectant mothers were repeatedly advised to continue planning for hospital deliveries, regardless of a crisis.

9. Competent pediatricians and obstetricians were to be kept available for consultation purposes as an aid to the general practitioner or to cover for him in case he was suddenly pressed into other disaster activities.

10. Prompt resumption of all obstetric and pediatric clinics was planned for as soon as circumstances possibly would permit.

HOW THE PLAN WORKED

With surprising ease, the obstetric load was carried with the minimum of friction. Postpartum patients were evacuated to their families without any protests. The delivery services and nursing facilities were adequate. The surprising fact, however, was that we did not get the flood of premature labors or abortions which were expected; there was a slight flurry the first day or two, but the incidence was hardly above normal. This can possibly be explained by two underlying factors: (1) The bombing came as a sudden surprise, giving us no time to develop the state of alarm that would accompany anticipation of such an event, and (2) the quality of American womanhood of today is such as to be able to face a real crisis with remarkable fortitude. The latter is an observation we have been able to make repeatedly in private and clinic cases and seems convincing that the mother of today instinctively retains some of the courage which allowed pioneer women to continue to rear their families in the face of hardship, privation and danger. However, it is fully appreciated that a second bombing here would be a much more severe test of fortitude than was the first and we are continuing to expect an increased load of abortions and premature labors in the event of another sudden bombing; the plans outlined are still being kept as a practical working basis.

WHAT WE HAD NOT PLANNED

It is hard to anticipate every eventuality ahead of time, and we found here that unexpected circumstances presented themselves, demanding solution. To mention a few:

1. The immediate and continued blackouts made night traveling difficult, slow and hazardous. Pregnant women who were developing symptoms of beginning labor were advised to get in touch with their physicians before nightfall and to enter the hospital during daylight hours as often as circumstances warranted. The radio and the press were used to disseminate such information.

2. The declaration of sudden martial law prohibited any one from being on the street at night except a few specially privileged classes. Police, taxicabs, doctors, civilian guards, aid station employees and ambulances were among the privileged classes. In the event of onset of labor at night, taxicabs and police patrol cars proved adequate for such transportation and the police radio patrol system proved efficient in locating the call of the pregnant woman with the minimum of delay.

3. A high percentage of our midwives proved to be aliens and were given no leeway in privileges of being on the street at night. They were quickly convinced that any of their patients going into labor at night would have to be referred to the nearest hospital as the only solution of that problem.

4. There was an abrupt increase in incidence of eclamptogenic toxemia. This is understandable when one realizes that a prolonged period of stress would tend to disrupt metabolism and throw a considerable extra load on the nervous system.

5. The question arose what to do with the early pregnant woman whose husband had suddenly been killed. There were numerous instances of women who had been severely shocked by the sudden loss of the husband in the unexpected catastrophe, added to which was the discovery of an early pregnancy. It was gratifying to note the renewed courage of each of these women when she was advised to carry through with her pregnancy for two logical reasons: (1) she would be able to have a living memory of her husband who died so gallantly and (2) she would be able to make a real contribution to the national program by bearing a child. I saw no hint of refusal to carry through after these facts had been carefully explained.

COMMENT

The experiences of managing a community wide obstetric program in Hawaii before, during and after a sudden major disaster are described in the hope that these facts may be of some value to other communities in their efforts to make similar plans. Previously made plans proved workable in an acute crisis, although several unanticipated problems arose which were solved without difficulty.

LATER.—Since the foregoing was written, Honolulu has had two air raid alarms and one bombing; the program outlined is still proving itself useful.

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THE VENOGRAPHIC DIAGNOSIS OF THROMBOPHLEBITIS OF THE LOWER EXTREMITIES

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Convincing evidence is rapidly accumulating that most pulmonary emboli of extracardiac origin arise from thrombophlebitis in the deep veins of the lower extremities.[1] The passage of an embolus from the leg to the lung can be prevented by division of the femoral vein. Indeed, Fine and Sears [2] have recently urged this procedure in all cases of deep thrombophlebitis of the lower extremity as the most effective prophylaxis against embolism. The prevention of pulmonary embolus depends on the early recognition of the venous thrombosis, but the clinical evidence of phlebitis may be equivocal or entirely lacking until a pulmonary infarct indicates its presence. A method which can establish the diagnosis and locate the side on which the process lies has been provided by the venographic technic recently described by Bauer.[3] The benefits of this diagnostic procedure are the subject of this communication.

TECHNIC

The patient lies on his back with a 6 cm. block heel. A 14 by 17 inch x-ray film [4] is placed under the leg, its lower edge about 3 inches above the ankle. A small incision is made about 1 cm. behind the external malleolus. A constant small vein is found here which communicates readily with the deep system. Through a fine needle 20 cc. of 35 per cent diodrast [4a] is injected at a uniform rate during a period of sixty seconds. At the end of the injection the exposure is made.

Resistance to the injection may be notably increased over that encountered in the absence of deep thrombosis. A useful hint of the presence of thrombosis is a decid-

From the Surgical Department of the Beth Israel Hospital.

1. Frykholm, Ragnar: Pathogenesis and Mechanical Prophylaxis of Venous Thrombosis, Surg., Gynec. & Obst. **71**: 307 (Sept.) 1940. Neuman, R.: Centers of Origin and Forms of Development of Thrombosis of the Leg, Virchows Arch. f. path. Anat. **301**: 708, 1938. Rössl, R.: On the Significance and Origin of Venous Thrombosis of the Lower Legs, ibid. **300**: 180, 1937. Hunter, W. C.; Sneeden, V. D.; Robertson, T. D., and Snyder, G. A. C.: Thrombosis of the Deep Veins of the Leg: Its Clinical Significance as Exemplified in Three Hundred and Fifty-one Autopsies, Arch. Int. Med. **68**: 1 (July) 1941. Fine and Sears.[2] Bauer.[3]

2. Fine, Jacob, and Sears, J. B.: The Prophylaxis of Pulmonary Embolism by Division of the Femoral Vein, Ann. Surg. **114**: 801, 1941.

3. Bauer, G.: Venographic Studies of Thromboembolic Disease, Acta chir. Scandinav. (supp. 61) **84**: 1, 1940.

4. Bauer uses a larger film.

4a. Supplied by the Winthrop Chemical Company.

edly increased caliber of the vein at the ankle. If the foot is held in moderate inversion the shadow of the veins will not be obscured by that of the bones of the leg. The normal venogram shows the deep veins of the calf, the popliteal and the femoral vein well outlined. A few superficial veins also are seen. Thrombophlebitis is characterized by partial or complete absence of filling of the deep veins with the contrast medium. Superficial collateral channels may be evident even in the acute stage, although they are more obvious in long standing deep thrombophlebitis. When the venogram of an extremity is repeated, the identical pattern of normal filling or of a filling defect is reproduced.

The value of this type of venography is illustrated in the following cases:

CASE 1.—A woman aged 35 entered the hospital complaining of recurrent attacks of upper abdominal pain of several years' duration. A Graham test was positive for cholelithiasis. Cholecystectomy and choledochostomy were done. The postoperative course was uneventful except for an unexplained daily

Fig. 1 (case 1).—Normal filling of deep system on both sides.

low grade elevation of temperature during the second week after operation. The leukocyte count varied between 12,000 and 15,000. Because of these signs deep phlebitis in the legs was suspected and looked for, but no evidence for this diagnosis could be found. Venograms were done on both lower extremities during this period and normal findings were obtained (fig. 1). On the nineteenth postoperative day the patient complained of pain in the left calf and pain in the right side of the chest. Examination disclosed tenderness in the left calf and dulness to percussion and rales at the right lung base. Bilateral venograms were repeated and showed failure of filling of the deep veins of the left leg (fig. 2). Division of the left common femoral vein was done. At operation, six hours after venography, diodrast was found in the femoral vein. No clot or thrombus was present at the site of division. Within twenty-four hours the pain and tenderness in the left leg disappeared completely. Three days later the patient was allowed to be up and about and was discharged a week after division of the femoral vein free from all symptoms and signs in the chest and extremities. There was no edema in either leg.

In this case the unexplained low grade fever aroused the suspicion of deep phlebitis, but in the absence of evidence to support this diagnosis the first venograms were taken and found normal. When these were repeated a week later following the appearance of pain in the leg and chest, a distinct change in the veins in the left leg was observed.

CASE 2.—A man aged 60 entered the hospital for the repair of a recurrent inguinal hernia. Examination disclosed hypertension, pulmonary emphysema and a right inguinal hernia. Herniorrhaphy was done, using fascia taken from the right thigh. The postoperative course was uneventful for twelve days. He was then allowed up in a chair. That evening he complained of pain in the left calf, which was found to be slightly tender on deep palpation. There was slight pain on dorsiflexion of the foot. There was no edema, cyanosis or increased heat. There was no elevation of temperature or pulse rate, and the leukocyte count was 10,700. A venogram of the left leg showed failure of filling of the deep system of veins (fig. 3). A venogram of the right leg taken for comparison showed normal filling of the deep veins. The small vein at the ankle on the left side was observed to have twice the diameter of the same vein on the right side, and there

Fig. 2 (case 1).—Second venogram of left leg showing acute thrombophlebitis with complete absence of filling of the deep veins of the lower leg, the popliteal vein and the lower part of the femoral vein. The greater and lesser saphenous veins are filled.

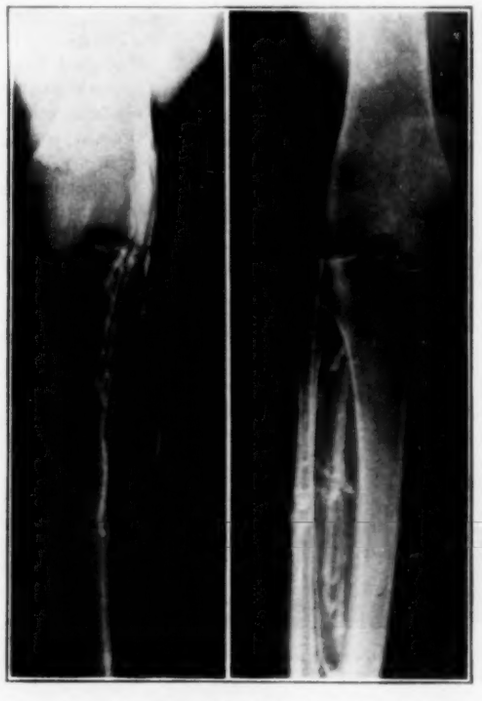

Fig. 3 (case 2).—Failure of filling of the deep veins below the popliteal is shown on the left. The superficial veins are larger and more numerous on this side.

was much more resistance to injection on the left side. The next morning the patient complained of a sudden onset of pain in the right side of the chest aggravated by inspiration. Rales, which were not present previously, were heard in the right lower lobe. A diagnosis of pulmonary infarction was made

and confirmed by a roentgenogram. Under local anesthesia the left femoral vein was divided just distal to the profunda femoris. The vein at this level appeared normal, but when it was divided diodrast escaped from its lumen. This was interpreted as being due to a greatly retarded blood flow from the veins blocked by thrombus. The patient became free from pain and tenderness in the leg within twenty-four hours after division of the vein. Later there was a small pleural effusion and evidence of infection in the infarcted area of the lung. Further progress was satisfactory until the twenty-third postoperative day, when after having been up and around he experienced severe pain in the left side of the chest followed by hemoptysis. Severe dyspnea and cyanosis developed. Examination showed rales and a friction rub in the left lower part of the chest and evidence of infarction in the left lower lobe, which was confirmed by roentgenography. Since the source of the second infarct was uncertain, venograms were again taken of both legs. The injection on the left side was made into the great saphenous vein in the midthigh, as suggested by Bauer, in order to outline the femoral vein proximal to the site of division as well as the iliac vein. The roentgenogram (fig. 4) showed normal filling of these structures. The venogram on the right side, however, disclosed an absence of filling in one of the tibial veins, and this was considered to be due to thrombosis (fig. 5). Accordingly, despite the patient's respiratory distress the right femoral vein was divided below the vena profunda under local anesthesia. Although convalescence from the pulmonary complication was somewhat stormy for a few days, recovery followed.

If left femoral vein ligation in this case had been done immediately after the venogram disclosed evidence of thrombosis, the first infarction might have been averted. When the second infarct occurred, further venography excluded thrombosis in the left common femoral and iliac veins and located the block in the right anterior tibial vein.

CASE 3.—A man aged 38 entered the hospital complaining of pain in the right side of the chest and cough of three weeks' duration. The history disclosed that asymptomatic varicose saphenous veins had been present for ten years in the right leg. These had been injected five years before admission. Physical examination was negative except for dulness and diminished breath sounds throughout the lower two thirds of the right lung field and varicosities of the saphenous system of the right leg. Roentgenograms of the chest showed a pleural effusion. Thoracentesis yielded grossly bloody fluid. Culture, Gram and Ziehl-Neelsen stains showed no bacteria. No tumor cells were found in the sediment of the centrifuged pleural exudate. Pulmonary infarction was considered in the differential diagnosis. Accordingly, the deep veins of the legs were investigated. No clinical evidence of deep phlebitis was apparent, but venography showed failure of filling of the deep system on the right side (fig. 6). The venogram of the left leg showed normal deep veins. The right common femoral vein was divided. No clot was found at the site of division, but diodrast escaped from the distal end of the divided vein as in the previous cases. The convalescence was uncomplicated. The pleural effusion gradually disappeared. Further x-ray studies disclosed no evidence of disease in the pulmonary parenchyma. The patient was discharged eight days after operation with no edema or disability in the legs.

Fig. 4 (case 2).—Venogram of left common femoral vein and iliac vein. This roentgenogram was taken after the injection of diodrast into the greater saphenous vein in the thigh, ten days after division of the femoral vein below the profunda. No evidence of disease of the veins is present.

In this case the only symptoms were pain in the chest and cough. The only significant physical findings were the superficial varicosities of the right leg and a bloody pleural effusion. Neoplasm, tuberculosis and the presence of pulmonary infarction were considered in the differential diagnosis. Despite complete absence of clinical evidence of phlebitis, venographic investigation of the legs gave clear evidence of an obstructive process in the deep veins of the right leg (fig. 6). The right femoral vein was divided to prevent the occurrence of further pulmonary infarction.

Fig. 4 (case 2).—Second venogram of right leg. The failure to outline the greater part of the anterior tibial vein by this venogram in contrast to the better filling shown by the previous venogram of the same leg (fig. 3) suggests the development of thrombosis in this vessel.

CASE 4.—A woman aged 40 entered the hospital complaining of urinary incontinence. She was obese and had hypertension. Two vaginal operations for incontinence were done in a period of two months. At the end of this time, when the patient was allowed out of bed, she complained of difficulty in walking because of pain in both calves, which were tender on pressure. A daily temperature elevation of 1 degree was noted, but there was also evidence of mild urinary sepsis. It was not clear whether or not the patient had deep phlebitis. Venograms showed normal filling of the deep veins of the legs (fig. 7). The patient was therefore allowed to continue to walk about, with gradual disappearance of the discomfort in the legs.

This patient's complaint of pain in the legs when first allowed out of bed and the low grade temperature elevation suggested the possibility of bilateral phlebitis, but the normal venograms provided the only assurance obtainable that she could be permitted to be active without fear of a pulmonary embolus.

COMMENT

Until recently venography has been unsatisfactory for the diagnosis of thrombophlebitis because the technics utilized were incapable of visualizing the entire deep system of veins. Since evidence is now available[1] that the source of most pulmonary emboli is thrombophlebitis in the deep veins of the lower leg, the venographic method of Bauer, which adequately visualizes

these veins,[5] provides the most reliable means of establishing the diagnosis when the signs and symptoms are inconclusive or wholly lacking. An extremely useful guide for the institution of prophylactic therapy for pulmonary embolism is thus provided.

The possibility of setting up thrombosis in the veins by injection of diodrast is probably not an important consideration in view of Bauer's experience and the absence of phlebitis following the use of diodrast for intravenous urography. A long exposure (twenty-four hours in one instance) of the intima of the femoral vein to diodrast has been observed without gross evidence of injury.

Phlebitis has not developed at the site of injection, even when it is repeatedly done. We have nevertheless adopted the suggestion of Dougherty and Homans [6] that the vein be washed out with saline solution after the injection of the diodrast. Another theoretical hazard, i. e. the release of a clot by the pressure of the injected fluid, has not occurred to our knowledge.

We have observed dilatation of the constant small vein at the ankle which is used for the injection in the presence of thrombophlebitis. We have also noticed increased resistance to the injection in the presence of thrombophlebitis.

The finding of diodrast in the femoral vein at the time of division is evidence of a retarded flow in the deep system of veins and provides indirect confirmation of the venographic diagnosis of thrombophlebitis.

There is frequently good reason for performing venography on both sides, not only to confirm or refute the clinical evidence on the side under suspicion, but also to demonstrate the presence or absence of the disease in the unsuspected side. It should be clear that

Fig. 6 (case 3).—The deep veins of the upper half of the right lower leg, the right popliteal vein and the right femoral vein do not fill. The venous return is by way of the varicose external saphenous vein.

the process is frequently bilateral and that an embolus may arise from either side whether or not signs and symptoms are present. The data provided by Bauer and our experience to date suggest that, when properly performed, a normal venogram can be regarded as conclusive evidence against thrombophlebitis in the veins visualized.

After operation patients commonly experience pain in the calves when they first begin to walk. In this situation a suspicion of phlebitis with its implied danger of embolism is unavoidable. Heretofore a guide to an intelligent choice of action has not been available. Fatal embolus just before or soon after discharge from the hospital occasionally results in such circumstances. By utilizing the venographic method under discussion a means of instituting preventive therapy is now possible.

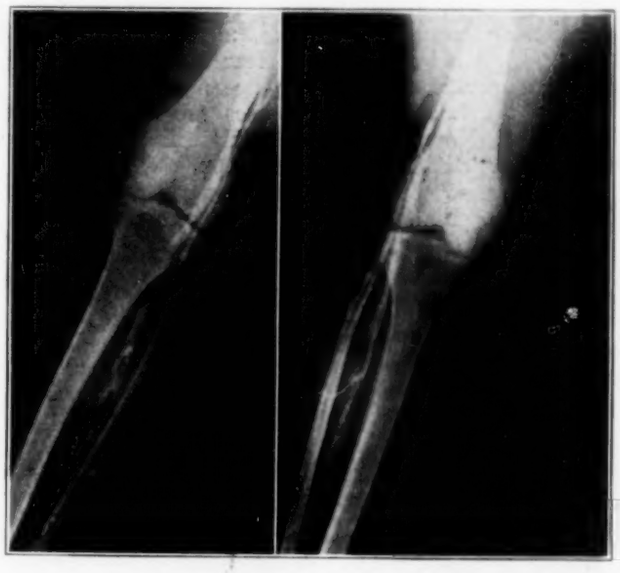

Fig. 7 (case 4).—The deep veins fill normally.

CONCLUSIONS

1. A technic described by Bauer for the visualization of the deep veins of the leg has been useful in the diagnosis of acute thrombophlebitis.

2. The early diagnosis of thrombophlebitis by this method facilitates the institution of effective prophylaxis against pulmonary embolism at an earlier period than has been possible heretofore.

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5. The method advocated by Dougherty and Homans [6] is substantially the same as that advocated by Bauer, although the former authors applied the method primarily for study of the veins in the thigh rather than the lower leg. Bauer emphasized the value of roentgenographic evidence in the lower leg for the diagnosis of acute thrombophlebitis. A 14 by 36 inch film and cassette is now available for filming the entire leg.

6. Dougherty, John, and Homans, John: Venography, a Clinical Study, Surg., Gynec. & Obst. **71**: 697 (Dec.) 1940.

Leadership.—If four men guess wrongly on a given prediction and the fifth man guesses rightly we say "how wise" when in reality we ought to say "how lucky." A guess that turns out right is not a prediction; it remains a guess. A man whose prediction is justified by future events need not necessarily have found the one solution possible. In much of science there is one answer and one answer only to a given problem. It is not plus or minus four but plus four and not minus four. In many social problems, on the other hand, the correct solution is the acceptable solution, the workable solution, and there may be several such solutions. Lincoln found his solutions by a method all his own. He himself disclaimed leadership. He said the people led. He waited until he thought that he knew what the people were thinking. There is another type of leadership that may be higher still, the type that teaches a people to understand what it ought to want. Only in conversation, using the term in its broadest sense, has this been done in American life, with conspicuous failures all too often in oil conservation, soil conservation, forest conservation.—Bowman, Isaiah: Enduring Purpose, *Assn. Am. Coll. Bull.* **26**:194 (May) 1940.

CHRONIC HEMOLYTIC STREPTOCOCCUS ULCERS OF THE EXTREMITIES

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It is indeed strange that chronic hemolytic streptococcus ulcers of the extremities have received so little attention and comment. This is all the more unusual since the lesion itself forms a clearcut entity and since there is a specific treatment for the condition.

There are but 5 of these cases reported in recent literature.[1] Nevertheless, 31 such cases were seen in the surgery clinic of the Indianapolis City Hospital during the past two and one-half years. The inference is obvious. Many chronic hemolytic streptococcus ulcers of the extremities have gone undiagnosed. In fact, none were found at the Indianapolis City Hospital until Goodman's [1] report in 1938.

DESCRIPTION

Since so many streptococcic ulcerations have recently been described, it is essential that a clearcut picture be given of the condition at hand. It bears no relation in appearance or course to the burrowing ulcers or symbiotic gangrene described by Meleney.[2]

The ulcer starts at the site of a slight cutaneous excoriation or insect bite. After a few days a small indolent ulcer appears. This is usually about 1 cm. in diameter but may progress slowly to 5 or 6 cm. in a week or two. Pain is not an outstanding feature.

The ulcer has none of the characteristics which suggest to the clinician the possibility of a hemolytic streptococcus infection. The tissue reaction is slight, being confined to the reddened ulcer margin. This may or may not be undermined. There is no surrounding edema or lymphangitis. The base of the ulcer weeps a watery serum from a pale atrophic granulation tissue. The lesion as a whole gives the impression that the tissues are making little or no effort to heal the defect.

Practically all the ulcers are found on the lower leg. In the present report only two were present on the hand.

The hemolytic streptococcus can be found in cultures from all ulcers, although it may not be identified on the first culture. This organism may appear in pure culture but most frequently has some contaminant. In the present report the contaminant was Staphylococcus albus in one half of the cases. These contaminating organisms are not considered to be growing in symbiosis with the hemolytic streptococcus.

There is one feature of the disease which is of considerable aid in suggesting the diagnosis. Most chronic ulcers have a definite background. They are superimposed on old varicosities, arteriosclerosis, frost bite or syphilis. This is not the case in chronic hemolytic streptococcus ulcer. This ulcer has no such background. It appears usually where there is no vascular impairment and where the circulation is quite adequate. It is seen most frequently in children and young adults. The average age at the Indianapolis City Hospital was 22.7 years. The oldest patient was 57, the youngest 3.

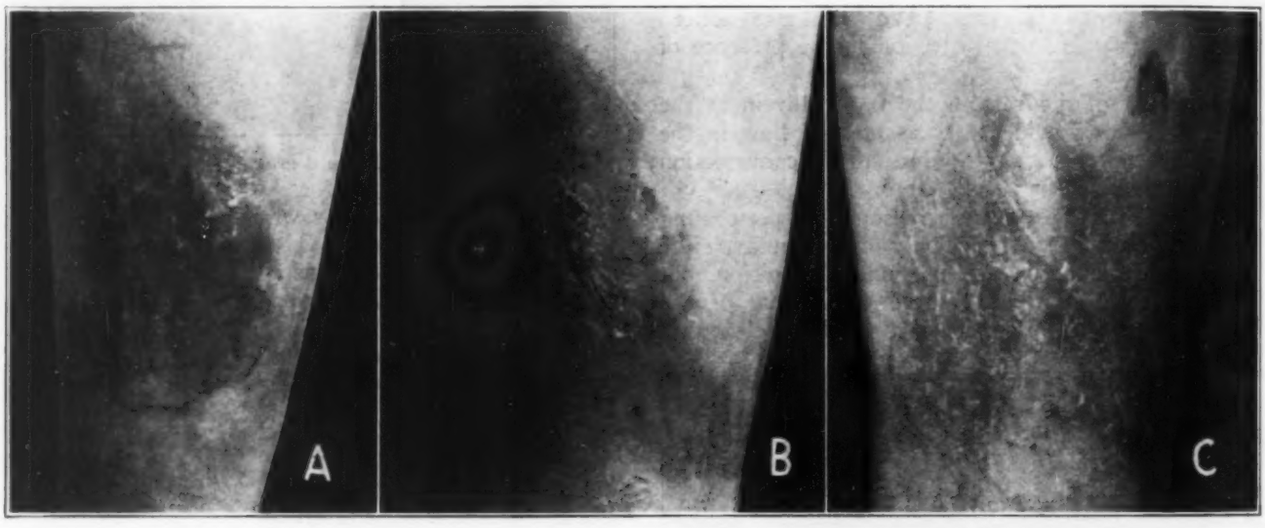

Fig. 1 (H. B., aged 40).—Ulcer and excoriation over anterior tibial region spreading under local treatment. This followed a bruise and slight abrasion two months prior to *A*. *B*, after eighteen days of sulfanilamide 60 grains (4 Gm.) daily. *C*, complete healing after dropping off of crust a few days later.

CASES

The cases identified and studied were seen in the outpatient surgical clinic of the Indianapolis City Hospital. No attempt has been made to list the cases separately. They have been summarized and the results noted. Three typical cases are shown in the accompanying illustrations. All cases were seen during the two and one-half year period starting in October 1938 and ending in April 1941.

During this time 52 chronic ulcers were studied. From these were obtained one or more cultures of the (beta) hemolytic streptococcus. Of this number there were 21 ulcers which were considered to have a definite background of vascular impairment or syphilis. These were dropped from the present study, leaving 31 cases in which the ulcer was thought to be due primarily to the hemolytic streptococcus. No other contributing cause could be found.

All ulcers appeared on the lower extremity with two exceptions. These were in children with several ulcers over the dorsum of the hand and arm. There were 2 instances in which more than 1 member of the same family had a chronic hemolytic ulcer at the same time.

From the Department of Surgery, Indianapolis City Hospital, and the Indiana University School of Medicine.

1. Goodman, M. H.: Chronic Streptococcic Ulcer of the Skin, J. A. M. A. **111**: 1427 (Oct. 15) 1938. Wright, C. S., and Friedman, Reuben: Chronic Streptococcic Ulcer of the Skin Responding to Sulfanilamide, Arch. Dermat. & Syph. **39**: 554 (March) 1939. Hamburger, H. J.: Observations on the Pathology and Therapy of the So-Called Frontier Sore, Indian M. Gaz. **74**: 151 (March) 1939.

2. Meleney, F. L.: Zinc Peroxide in the Treatment of Microaerophilic and Anaerobic Infections, Ann. Surg. **101**: 997 (April) 1935.

Two patients were admitted to the hospital for treatment. The rest were handled entirely as outpatients. All cases were followed, and so far there have been no recurrences in the primary hemolytic streptococcus ulcer group.

The ulcers varied in size from 1 cm. to 6 cm. Local adjacent skin inflammation or edema was found in only 5 instances. The remaining cases merely showed an indolent sluggish ulcer with little or no reaction.

The patients had had their lesions for from two weeks to four years when specific therapy was started in the hospital. Omitting the four year case, the average duration of the ulcer was two months. During this time they had received all types of home remedies plus those used currently in the clinic. The use of the latter drugs depended on the whim of the particular clinician. They included 2 per cent methylrosaniline (gentian violet), tincture of merthiolate, scarlet red ointment, boric acid ointment, zinc oxide ointment, ammoniated mercury ointment, wet dressings of physiologic solution of sodium chloride, magnesium sulfate, Burow's solution, diluted solution of sodium hypochlorite, 70 per cent alcohol and dusting powders of thymol iodide and sulfanilamide.

TREATMENT

The lesion usually received varying amounts of the foregoing drugs. Then some one usually became curious as to why healing did not take place and finally took a culture. When a positive culture was obtained, specific therapy was instituted.

Specific therapy consisted of oral sulfanilamide as suggested by Goodman.[1] The adult dosage varied from 20 to 90 grains (1.3 to 6 Gm.) daily. In general the smaller doses were ineffectual but doses of from 60 to 70 grains (4 to 4.5 Gm.) daily seemed quite sufficient.

The patients were followed in the outpatient clinic to guard against untoward reactions. Blood counts were not followed on all the patients, but this is a precaution which certainly should not be overlooked.

Occasional blood sulfanilamide determinations were made. These were rather low, varying from 3.5 to 5.2 mg. per hundred cubic centimeters of blood. Apparently no greater concentration was necessary in this type of infection.

RESULTS

There were 5 of the 31 cases of primary chronic hemolytic streptococcus ulcer which healed under local wet dressings and applications. These healed in an average of fourteen days.

Six more patients received entirely inadequate amounts of sulfanilamide. Several of these were lost temporarily to the clinic and continued with local home remedies. Their ulcers eventually all closed in an average of fifty-one days.

This leaves 19 patients who received adequate amounts of sulfanilamide. These patients had had their ulcers for from two weeks to four years. Omitting the case of four years' duration, they had had their ulcers for an average of seven and seven-tenths weeks. Following the specific drug therapy the ulcers were healed in an average of one and eight-tenths weeks.

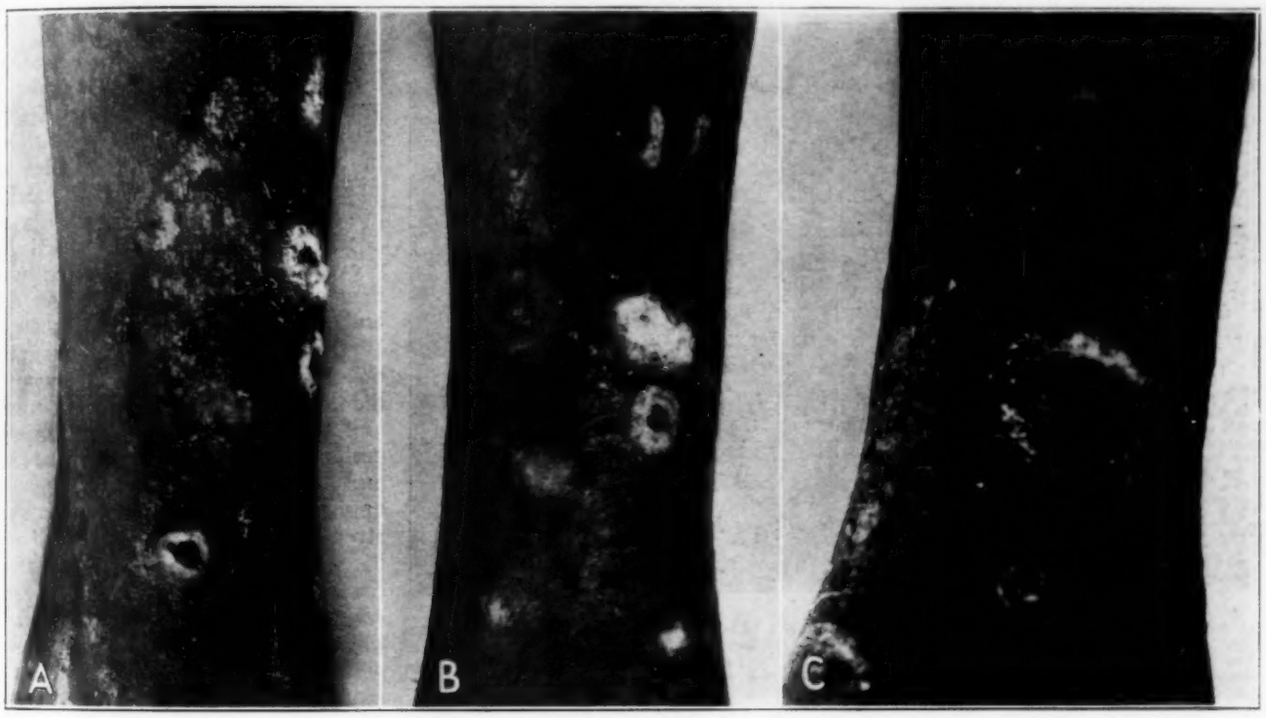

Fig. 2 (W. Y., Negro aged 26 years).—*A*, ulcers present for four years and being treated regularly in the surgical clinic. When cultures were finally taken and hemolytic streptococci found, 10 ulcers were present. *B*, after two days of sulfanilamide, ulcers showed signs of healing with healthy granulations. *C*, ulcers completely healed after fourteen days of sulfanilamide 60 grains (4 Gm.) daily.

The dramatic rapidity with which some of these chronic ulcerations heal is nicely shown in figure 2. The ulcerations had been present in this 26 year old Negro for four years. During most of that time he had been seen in the surgical clinic several times a week. During that time he had received every type of ointment and solution on the dressing table. At the time the condition was finally recognized, he had 10 ulcers measuring from 1 to 2 cm. in diameter. He was given 60 grains (4 Gm.) of sulfanilamide daily for fourteen days. At the end of this period the ulcers were completely healed for the first time in four years. They have remained healed.

The rapidity of healing under specific therapy is one of the most striking features of these ulcers. It is indeed thrilling to see them literally heal before one's eyes.

What has been said about the specificity of sulfanilamide holds true only for primary chronic hemolytic streptococcus ulcers and not for all chronic ulcers which contain this organism. During the course of the present study 21 ulcers were encountered which contained hemolytic streptococci but had as their basis varicosities, phlebitis, arteriosclerosis or syphilis. These patients were given sulfanilamide. The result was a disappearance of the hemolytic streptococcus, but the fundamental background of the ulcer still persisted and so did the ulcer.

One of the cases which was considered clinically and bacteriologically to be typical of chronic hemolytic streptococcus ulcer failed completely with sulfanilamide. Under this therapy the hemolytic streptococcus disappeared but the ulcer persisted. No other background could be found in this patient. The ulcer finally healed on home remedies one month after the patient left the hospital. It is possible that a fungous infection was an added factor here, though laboratory findings are lacking. Nevertheless this case represents a flat failure, since it answered all the requirements of the chronic hemolytic streptococcus ulcer.

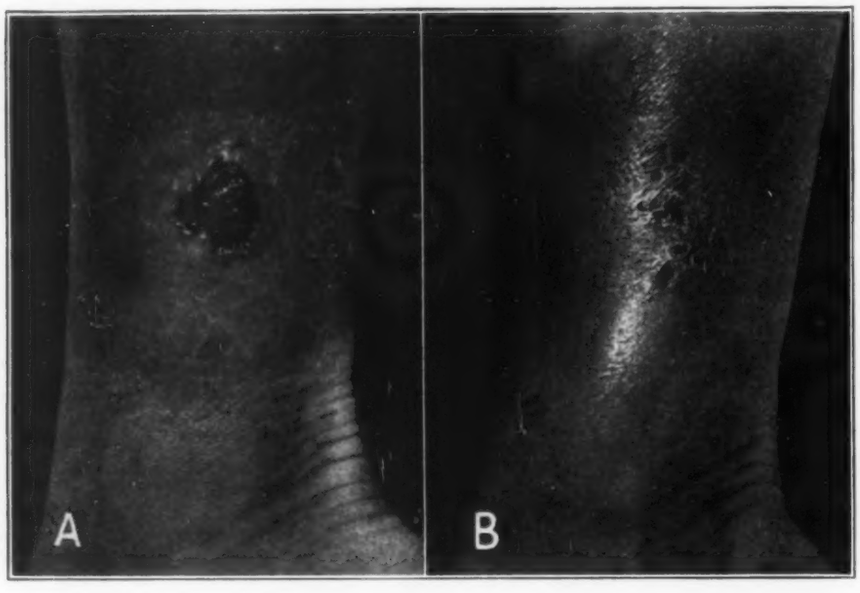

Fig. 3 (M. R., aged 41).—*A*, chronic ulcer of anterior tibial region containing hemolytic streptococci. Duration, one and one-half years. The ulcer had a vascular background following an injury. The patient could not tolerate oral sulfanilamide and so the powder was applied locally. Hemolytic streptococci had disappeared from the wound when a culture was taken three weeks later. *B*, complete healing after forty days of powdered sulfanilamide locally and no other type of therapy.

COMMENT

It must be emphasized that chronic hemolytic streptococcus ulcer is a very distinct entity and one which is rather frequently encountered. The oral use of sulfanilamide is specific for the lesion. This is true with the exception of an occasional case which is either resistant or more probably misdiagnosed. Among the present series there was 1 such case in 19 in which adequate doses of sulfanilamide were administered. Healing in the remaining cases was spectacular.

The hemolytic streptococcus was also cultured from a large group of varicose and other vascular ulcers. Of course, in these instances sulfanilamide did not cure the lesion. It did, however, cause considerable improvement. The suggestion is therefore made that, in vascular ulcers containing hemolytic streptococci, sulfanilamide be used as an adjunct to other forms of therapy. The drug, of course, would be useless when the organism is not present.

An interesting feature in epidemiology is noted in this Indianapolis City Hospital series. Of the 31 cases of primary chronic hemolytic streptococcus ulcer 27 (87 per cent) had their onset in the last six months of the year. This does not mean that this number were all treated during this period but that 87 per cent started from a scratch, abrasion or insect bite which was received between the first of June and the last of December. No adequate explanation has been found for this seasonal incidence. The contagious nature of the lesion is indicated by the fact that five ulcers occurred in two families. Three members of one family had ulcers at the same time, as did two in a second family.

In the cases here reported sulfanilamide was given orally. It is interesting to speculate on the possibility of applying the powdered drug directly on the local wound. It would seem to be an ideal situation for such use. The truth is that the oral use has been so completely satisfactory and specific that those in charge were loath to make the change. The drug was used locally in treatment of 1 patient with a vascular background caused by previous trauma. The ulcer was over the right anterior tibial region and measured 4 cm. in diameter. It had been present for one and one-half years. From the wound the specific organism was cultured and the patient started on sulfanilamide. This proved too toxic to him and so the powdered drug was applied locally. The hemolytic streptococcus had disappeared from the wound when cultures were taken three weeks later and the ulcer was completely healed at forty days (fig. 3). It is planned to use powdered sulfanilamide locally in subsequent cases of primary chronic hemolytic streptococcus ulcer.

SUMMARY

1. Chronic hemolytic streptococcus ulcers of the extremities constitute a definite entity with a specific therapy.

2. The lesion is characterized by its chronicity, similarity to chronic ulcers having vascular backgrounds, and lack of inflammatory reaction which might suggest its true nature. Usually it is seen in children and young adults with no vascular impairment. Diagnosis is confirmed by the culture of hemolytic streptococci from the ulcer. In no way does it resemble the symbiotic burrowing streptococcus ulcers.

3. Only 5 chronic hemolytic streptococcus ulcers have been reported in recent literature. None were seen at the Indianapolis City Hospital until a search was made for them. Thirty-one such cases were seen and treated in this institution in the past two and one-half years. The deduction is obvious.

4. This type of ulcer may heal under local treatment. Usually it does not. Oral sulfanilamide is specific.

5. There were 19 cases in the present series in which adequate amounts of sulfanilamide were given. These ulcers healed completely in an average of one and eight-tenths weeks, although they had first been treated locally with all types of drugs for an average of seven and seven-tenths weeks.

6. The local use of powdered sulfanilamide would seem to be indicated in this type of lesion, though it was not used in the present series.

7. It is suggested that cultures be taken of all chronic ulcers of the extremities to identify those belonging to the chronic hemolytic streptococcus group. In chronic ulcer cases with a vascular background and containing hemolytic streptococci, sulfanilamide might well be employed as an adjunct to other forms of therapy.

23 East Ohio Street.

OBSERVATIONS ON THE "EGG WHITE INJURY" IN MAN

AND ITS CURE WITH A BIOTIN CONCENTRATE

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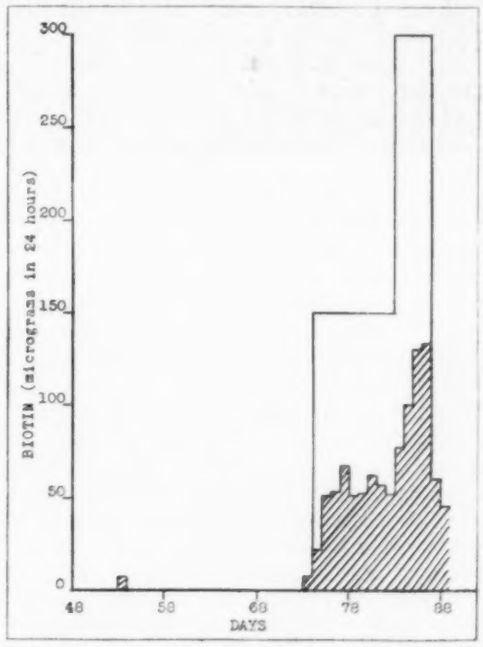
Many investigators have noted that the inclusion of large amounts of egg white in special experimental diets causes a definite nutritional disease in animals. This disorder, commonly called egg white injury, has for its chief symptom an "eczematous dermatitis" which can be prevented or cured by a protective substance formerly called vitamin H which is present in certain foodstuffs. There appears frequently in rats, in addition to the severe general eczematous dermatitis involving the eyelids and lips, an ischemic gangrene of the tip of the tail, presumably due to local vasoconstriction. Recent reports [1] have indicated that vitamin H is identical with biotin, a yeast growth factor, and also with coenzyme R, a growth and respiration factor for many strains of the legume nodule organism Rizobium. Williams and his co-workers [2] have demonstrated that the so-called egg white injury is due to an induced biotin deficiency caused by the binding of the dietary biotin by a protein fraction of raw egg white "avidin," thereby preventing the absorption of this vitamin from the intestinal tract.

In chicks a scaly dermatitis not due to pantothenic acid deficiency has been cured by vitamin H concentrates,[3] while biotin concentrates have protected turkey poults against a specific dermatitis.[4] It appears that this vitamin is also involved in the graying of fur in rats and mice [5] as well as in the synthesis of lipids by the rat.[6]

In view of the growing significance of biotin in animal nutrition, it seemed important to determine whether any of the phenomena of human deficiency disease might be related to biotin deficiency. To this end a small group of volunteers ate a diet planned to contain a minimal amount of biotin, which was composed of rice 125 Gm., patent white flour 80 Gm., farina 75 Gm., cane sugar 205 Gm., lard 32 Gm., washed butter 10 Gm. and lean beef 25 Gm. To this was added 200 Gm. of dehydrated egg white. The basal components represented 387 Gm. of carbohydrate, 31 Gm. of protein and 32 Gm. of fat, with a total caloric value of 1,960. In addition, 928 calories was derived from the 160 Gm. of protein and 32 Gm. of fat of the egg white for a grand total caloric value of 2,888. As the egg white was given in solution in a one-third aliquot with each meal, the percentage of egg white of the total food ingested daily was dependent on the amounts of the other components consumed. Usually the egg white furnished in excess of 30 per cent of the total daily caloric intake. Such a diet is poor in vitamins of the B complex except for riboflavin, which is present in desiccated egg white in amounts approximating 10 mg. per hundred grams.[7] Consequently the following vitamin supplement was given daily: thiamine hydrochloride 6 mg., riboflavin 9 mg., nicotinic acid 75 mg., pyridoxine 5 mg. and calcium pantothenate 5 mg. In addition, ascorbic acid 75 mg., vitamin A 5,000 units, ferrous sulfate 1 Gm. and calcium lactate 1 Gm. were given.

Of seven volunteers, it has been possible to continue 4 under observation to a satisfactory conclusion. Three were white men, the fourth a Negro woman. All were in good general condition and free from symptoms and signs of avitaminosis when the experiment was begun. During the third and fourth weeks all 4 subjects developed a fine, scaly dermatitis which did not itch and



Excretion of patient 3: shaded area, biotin excretion; unshaded area, biotin administered.

The authors were given constant help and valuable suggestions by Dr. R. E. Butler and technical assistance by Mrs. Marjorie Bee.
This investigation was made possible by grants in aid by the John and Mary R. Markle Foundation and an anonymous donor, and by donations of vitamins by many manufacturers.
From the University of Georgia School of Medicine and University Hospital (Drs. Sydenstricker, Singal, Briggs and DeVaughn) and the National Institute of Health (Dr. Isbell).

1. du Vigneaud, Vincent; Melville, D. B.; György, Paul, and Rose, Catherine S.: Science **92:** 62 (July 19) 1940. György, Paul; Rose, Catharine S.; Hofman, Klaus; Melville, D. B., and du Vigneaud, Vincent: Science **92:** 609 (Dec. 27) 1940.
2. Eakin, R. E.; McKinley, W. A., and Williams, R. J.: Science **92:** 224 (Sept. 6) 1940. Eakin, R. E.; Snell, E. E., and Williams, R. J.: J. Biol. Chem. **136:** 801 (Dec.) 1940. György, Paul; Rose, Catharine S.; Eakin, R. E.; Snell, E. E., and Williams, R. J.: Science **93:** 477 (May 16) 1941.
3. Hegsted, D. M.; Oleson, J. J.; Mills, R. R.; Elvehjem, C. A., and Hart, E. B.: J. Nutrition **20:** 599 (Dec.) 1940.
4. Patrick, H.; Boucher, R. V.; Dutcher, R. Adams, and Knandel, H. C.: Proc. Soc. Exper. Biol. & Med. **48:** 456 (Nov.) 1941.
5. György, Paul, and Poling, C. E.: Proc. Soc. Exper. Biol. & Med. **45:** 773 (Dec.) 1940.
6. McHenry, E. W., and Gavin, Gertrude: J. Biol. Chem. **140:** lxxxvii (July) 1941.
7. Personal communication to the authors from Armour & Co., Chicago.

which disappeared spontaneously. Thereafter nothing of significance was noted until the seventh week, when 1 patient developed a maculosquamous dermatitis of the hands, arms and legs. During the seventh and eighth weeks all patients showed a striking grayish pallor of the skin which was out of proportion to the blood picture and was interpreted as evidence of peripheral vasoconstriction. During the same period the 3 white patients showed definite atrophy of the lingual papillae, patchy with the production of a "geographic" tongue in 1, general in 1 and affecting the lateral thirds of the tongue in the third. The Negro patient showed no tongue changes until the fourteenth week of the experiment, when rather rapid denudation of the tongue began. It was notable that the tongues of these patients remained pale with none of the capillary engorgement seen in pellagra or ariboflavinosis. During the ninth and tenth weeks all patients showed dryness of the skin of the extremities with well defined reticulation and a tendency again to fine, branny desquamation; this dermatosis was very similar to that observed during the early period of the experiment. No ocular or genital lesions were observed.

After the fifth week prominent symptoms were strikingly similar to those reported for experimental thiamine deficiency. Mild depression progressed to extreme lassitude, somnolence, hallucination in 1 patient and a mild panic state in 2. Muscle pains, hyperesthesia without demonstrable neurologic changes and localized paresthesias occurred in all 4 subjects. No definite reflex changes were observed. Anorexia progressed to nausea and sitophobia. It was extremely difficult to get these subjects to continue the diet. The caloric intake fell off rapidly in all during the last three weeks of the experiment. Two patients with electrocardiographic evidence of coronary ischemia had precordial pain. The electrocardiograms could not be differentiated from those attributed to thiamine deficiency.

Examinations of the blood at weekly intervals showed a definite diminution in the hemoglobin content, the number of erythrocytes and particularly the volume of packed red cells. These changes occurred in spite of a theoretically adequate intake of iron and a very large protein fraction in the diet. All 4 patients showed an increase in bile pigments and cholesterol in the blood.

Determination of biotin excretion in the urine showed that at the end of seven and eight weeks of the experimental regimen the subjects excreted from 3.5 to 7.3 micrograms of biotin in twenty-four hours as compared with the excretion of 29 to 62 micrograms by persons taking a normal diet.[8]

Treatment with an injectable biotin concentrate[9] has been completed in 3 of the 4 experimental subjects. The daily dose has varied from 75 to 300 micrograms. The minimal amount required for prompt relief of symptoms seemed to be 150 micrograms daily. Depression, muscle pain, precordial distress and anorexia have been abolished on the third to fifth day of treatment. Striking relief of depression amounting almost to euphoria occurred in 2 patients. Active distaste for the diet was replaced by willingness, even eagerness, to eat it although there was no significant increase in the amount consumed. The striking ashy pallor disappeared in four days. Insufficient time has elapsed for evaluation of other evidences of correction of physiologic disturbances.

Immediately after the administration of 150 micrograms of biotin concentrate the urinary excretion rose rapidly from a deficiency level of 3 to 7 micrograms a day to a level approximating 55 micrograms. This level was maintained until the dose was increased to 300 micrograms a day, when there was a further stepwise increase in biotin excretion to a level approximating 140 to 150 micrograms daily with an immediate fall to a level slightly lower than those found in patients eating a normal diet when medication was discontinued. The excretion chart of patient 3 is typical of the patients observed.

SUMMARY AND CONCLUSIONS

In observations on human subjects maintained on a diet very poor in all vitamins of the B group except riboflavin supplied by egg white, supplemented with adequate amounts of available synthetic vitamins, in which at least 30 per cent of the total calories were supplied by desiccated egg white, definite symptoms and signs were produced.

Symptoms and signs were rapidly cured by the parenteral administration of a biotin concentrate in doses representing 150 to 300 micrograms of biotin per diem.

The phenomena observed were similar to some of those seen in spontaneous avitaminoses.

8. Biotin determinations were done by Dr. Isbell of the National Institute of Health.

9. Biotin concentrate was supplied by the S. M. A. Corporation, Chagrin Falls, Ohio.

AGNOGENIC MYELOID METAPLASIA OF THE SPLEEN

REPORT OF FIVE CASES ILLUSTRATING DIAGNOSTIC DIFFICULTIES AND THE DANGER OF SPLENECTOMY AND RADIATION THERAPY

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The clinical picture of splenic enlargement with anemia has always been of great interest to the internist, the surgeon and the pathologist. This syndrome is observed from infancy up to old age and is associated with many different conditions, most of which are little understood although they are characterized by definite names. Thus we have only to enumerate such names as erythroblastosis fetalis, Cooley's anemia, chronic subleukemic myelogenous leukemia, splenic anemia and Hodgkin's disease. Each one brings to mind a rather definite clinical and pathologic picture, and yet there are many so-called atypical cases in which the disease defies classification both during life and after death of the patient.

In a recent report Jackson, Parker and Lemon[1] integrated as a clinical entity a syndrome characterized by splenic enlargement and the presence of immature red and white cells in the blood. This condition is often erroneously diagnosed as chronic myelogenous leukemia, splenic anemia, erythroblastosis or Hodgkin's disease. Frequently the picture is so confusing that a splenectomy is performed, with unfavorable results.

It is our purpose in this communication to cite briefly 5 additional cases of this disorder and to point out the diagnostic errors, both clinical and pathologic, which were made until the picture was finally clarified.

1. Jackson, Henry, Jr.; Parker, Frederic, Jr., and Lemon, H. M.: New England J. Med. **222**: 985 (June 13) 1940.

As a final check, our clinical and pathologic material was passed on by Jackson and Parker; so we are sure that we are dealing with the condition described by them.

REPORT OF CASES

CASE 1.—Y. J., a white man aged 52, an electrician, first admitted to the hospital on Jan. 14, 1935, had had ten teeth extracted six months prior to admission and afterward had noticed shortness of breath on mild exertion, generalized weakness and night sweats. The sweats were constant, occurring one or two hours after midnight every night. The weakness had become more severe during the last two months.

His past history included gonorrhea twenty years and a fracture of the ankle twenty-two years before admission; otherwise his general health had been good. The family history was irrelevant.

Physical examination showed that he was well developed and nourished but appeared chronically ill. There was no icterus. The skin was of fair turgor and gave evidence of some loss of weight. It had a peculiar, waxy, light yellow tinge. The mucous membranes of the mouth were pale. The heart showed a soft systolic murmur at the apex which was not transmitted. The spleen was greatly enlarged, extending medially to the umbilicus and 4 fingerbreadths below the umbilical line on the left. No axillary, cervical or inguinal adenopathy was noted. The remainder of the physical examination was negative.

On January 17 examination of the blood showed hemoglobin 46 per cent, red blood cells 2,500,000, white blood cells 7,600, mature polymorphonuclear leukocytes 69 per cent, band cells 5 per cent, young forms 2 per cent, lymphocytes 5 per cent, monocytes 9 per cent, myelocytes 6 per cent, promonocytes 2 per cent, eosinophils 1 per cent, basophils 1 per cent, reticulocytes 5 per cent and platelets 150,000. There were severe poikilocytosis and anisocytosis, and many nucleated red blood cells were seen.

The following day a sternal puncture was done which gave no evidence of leukemic infiltration. A fragility test of the red cells showed that hemolysis began in a 0.425 per cent salt solution and ended in a 0.350 per cent salt solution. The Wassermann reaction was negative.

A roentgenogram of the chest showed a cardiac shadow large in all diameters. The lungs showed no evidence of tuberculosis or metastases. A flat film of the abdomen showed a shadow in the left upper quadrant and gave evidence of slight enlargement of the liver.

It was felt that the patient might benefit by splenectomy, provided the hemoglobin level could be raised preoperatively by transfusion, since the removal of such a large spleen would probably cause a great blood loss. Accordingly, the patient received three transfusions of 500 cc. of blood at three day intervals. After the last transfusion he had a reaction, the temperature rising to 104.2 F. Hemoglobinuria was not noted. The liver became somewhat enlarged during the ten days. The preoperative hemoglobin content was 60 per cent and the red cell count 3,200,000.

On February 7 splenectomy was performed with the patient under spinal anesthesia. The preoperative diagnosis was a tentative one of Banti's disease. The patient withstood the procedure well. The spleen weighed 2,850 Gm. The serosa of the spleen was free from adhesions. The surface was for the most part mottled red and reddish brown. There were also some irregular, scattered, dark purplish areas and a number of contracted, linear, yellow areas. The largest of these areas measured 2.2 by 0.4 cm. and on section showed irregular, yellowish, contracted tissue about which were some purplish petechiae. This tissue was firmer than the surrounding splenic substance. On the lateral surface was an irregular, orange red, slightly raised area 3.5 by 1 cm. Section through this area showed orange red tissue which extended in an irregular pattern down about 3.5 cm. and was firm, granular and shiny. Other sections of the cut surface were granular, shiny and reddish brown.

Microscopically the spleen showed typical myeloid metaplasia with numerous megakaryocytes and hemochromatosis.

The patient lived five years after splenectomy. In that time he had more than twenty separate hospital admissions and received more than fifty blood transfusions. His complaints were always essentially the same: dyspnea, weakness and night sweats. The last year before death dependent edema developed, and he eventually died from cardiac failure and terminal endocarditis.

Autopsy showed advanced osteosclerosis of all bones, particularly the femur, tibia and skull cap. Microscopically there were no changes indicative of leukemia in liver, kidney or marrow. The lymph nodes showed extreme infiltration with megakaryocytes without leukemic changes. There were extramedullary areas of hemopoiesis in liver and lymph nodes. There was also evidence of hemosiderosis in the pancreas and liver. The heart was enlarged and showed evidence of myocardial degeneration.

CASE 2.—T. F., a Russian woman aged 44, a dressmaker, was first admitted to the hospital on Oct. 14, 1938. Eight years before an enlarged spleen had been discovered during a routine examination for a "nervous breakdown." At that time she was in another hospital for one week, where the diagnosis of myelogenous leukemia was made. She was followed by the outpatient department for a number of years. No roentgen therapy was given because of a persistently low white cell count.

Since that time she had felt an increasing weight and sense of pressure in the left side of the abdomen. She had lost about 6 pounds (2.7 Kg.) in the last eight years. For the past two years her appetite had been poor and she practically always felt nauseated. Two and a half months before admission she had had a bout of vomiting with diarrhea following the ingestion of soft shelled crabs. She was seen by her physician, who sent her to another hospital for a transfusion, after which she felt better. She entered Lenox Hill Hospital after this for further study.

Her past history included diphtheria at the age of 15, with no sequelae, and a progressive scoliosis first noted at the age of 12, for which she was put in a plaster cast without any curative result. Her last menstrual period had been at the age of 43, a year prior to admission. She had been pregnant twice, once ten years and once eight years before admission. Both pregnancies were terminated for pernicious vomiting. The remainder of her past history was not significant. The family history was noncontributory save that two sisters had had "thyroid trouble."

Physical examination showed that the patient was poorly developed but fairly well nourished. The skin and mucous membranes were pale. The thyroid was somewhat enlarged along the lower margin, with a firm strip of tissue across the neck. No palpable cervical glands were present. The heart and lungs were normal. The thorax was asymmetrical. The spine showed scoliosis to the right, with the maximum curvature at about the fifth thoracic vertebra. There was moderate lordosis of the thoracic portion of the spine, with flaring of the right scapula. The entire left side of the abdomen was occupied by a smooth, firm, ovoid mass extending from the costal margin to below the iliac crest and from the midaxillary line to 3 cm. beyond the midline. There was moderate tenderness in the epigastrium medial to the mass and in the right upper quadrant. The edge of the liver and the kidneys were not palpable.

The hemoglobin content was 75 per cent, the red blood cell count 3,600,000 and the white cell count 13,800, with the following differential count: mature polymorphonuclear leukocytes 42 per cent, band cells 11 per cent, young forms 14 per cent, lymphocytes 22 per cent, monocytes 8 per cent, eosinophils 2 per cent and basophils 1 per cent. The red cells showed anisocytosis, poikilocytosis and polychromasia. There were 2 normoblasts per hundred white cells. Another differential count five days later showed 13 per cent myelocytes, 5 per cent myeloblasts and 2.7 per cent reticulocytes. Hemolysis of the red cells began in a 0.375 per cent solution, showing an increased fragility.

Roentgen examination of the chest showed scoliosis, but no mediastinal lymph node enlargement was seen. Roentgenograms of the long bones showed no osteosclerosis.

Since the diagnosis was doubtful and the presenting complaint was the discomfort caused by the spleen, peritoneoscopy

and a splenic biopsy were performed. These ruled out the possibility of leukemia or Hodgkin's disease but did not result in a definite diagnosis. The pathologic diagnosis from the biopsy was "probable neoplasm of the spleen." Accordingly, the patient was given a transfusion of 500 cc. of whole blood preoperatively, and on November 14 splenectomy was done, followed by a postoperative transfusion of 300 cc. She did fairly well and was discharged two weeks after splenectomy.

The spleen weighed 1,800 Gm. The surface was firm, gray red and glistening. On section there was a slightly increased resistance to the knife. Scattered over the cut surface there were many slightly raised, fairly well circumscribed, yellow red nodules measuring 0.3 to 1.2 cm. in diameter which were somewhat firmer than the surrounding tissue.

Microscopically the spleen showed myeloid metaplasia with many megakaryocytes, nucleated red blood cells, compression of the malpighian corpuscles, which were few in number, and but little fibrosis.

The patient has had five subsequent admissions since removal of her spleen:

From November 8 to November 16 the patient entered because of severe epistaxis which could not be controlled at home by packing. This subsided after conservative treatment and one transfusion. While she was in the ward, a vesicular eruption developed on an erythematous base over the left forearm and chest. Biopsy was done of material from one lesion, and the condition was diagnosed folliculitis cheloidalis.

From Jan. 5 to Jan. 20, 1940 the patient returned because of abdominal cramps and diarrhea. There was no evidence of any acute abdominal condition. The hemoglobin content was 60 per cent, the red cell count 2,500,000 and the white cell count 16,000. There were many nucleated red cells. A gastrointestinal series was done and showed no pathologic conditions. The patient was given one transfusion and discharged.

From May 20 to May 21 the red cell count was 1,800,000, the hemoglobin content 41 per cent and the white cell count 18,700. The patient entered this time for a transfusion. She had been well, except for nocturnal pain in the chest radiating through to the back and progressive fatigue since her last admission.

From July 26 to July 30 the patient entered again for transfusion, complaining of weakness and fatigue. Physical examination showed the liver to be enlarged to the umbilicus for the first time. The heart showed a loud, blowing systolic murmur and gallop rhythm. The gallop rhythm disappeared after two 500 cc. transfusions. The reflexes were generally hyperactive throughout, and there was a transient ankle clonus present. She was somewhat improved on discharge. On admission the blood showed hemoglobin 25 per cent, red cells 1,200,000 and white cells 13,200. The smear showed many normoblasts.

November 19 to November 23 the patient was well until ten days before admission, when she had a severe, persistent, unilateral headache and had become progressively weaker during the preceding seven days. The hemoglobin content was 20 per cent, the red cell count 1,100,000 and the white cell count 9,700, with many normoblasts present. The icterus index was 5.0. A roentgenogram showed no osteosclerosis at this time. The fragility test showed hemolysis beginning in a 0.375 per cent salt solution and completed in a 0.300 per cent salt solution. The patient was somewhat improved on discharge.

The patient was readmitted on Feb. 4, 1941 with weakness and severe anemia. The blood showed a hemoglobin content of 8 Gm., 2,200,000 red cells and 4,800 white cells, with 37 per cent neutrophils, of which 5 per cent were nonfilamented, 46 per cent lymphocytes, 16 per cent monocytes and 1 per cent basophils. Platelets were normal. There were 4 per cent nucleated red cells per hundred white cells.

The bone marrow showed fibrosis. The remaining marrow was normal in cellular constituents. The patient was given two transfusions of 500 cc. of whole blood and discharged improved.

CASE 3.—M. E., an Austrian woman aged 48, entered the hospital on Dec. 16, 1937 because of a progressive weight loss of 22 pounds (10 Kg.) during the preceding year, along with frequent watery stools, occasional tarry stools, and the intermittent passage of worms varying in length from 1 to 2 inches (2 to 5 cm.). She had had moderate anorexia during the few months before admission. She had not consulted a physician for these symptoms.

Her past history revealed that catamenia had ceased a little more than a year previously, with only one episode of vaginal bleeding, lasting eight days and accompanied by pelvic discomfort, thirteen months before. Otherwise the past history and the family history were noncontributory.

Physical examination showed that the woman was chronically ill, with slightly jaundiced scleras. There was no lymphadenopathy. The heart had a loud systolic murmur best heard over the base, with a blood pressure of 128 systolic and 60 diastolic. The entire left side of the abdomen was filled by a firm mass extending to the level of the umbilicus. No nodules were felt. The liver was likewise enlarged in the region of the flank to the level of the umbilicus.

Examination of the peripheral blood revealed hemoglobin 80 per cent; the red blood cell count was 4,200,000 and the white cell count 10,800 of which the differential count was mature polymorphonuclear cells 81 per cent, band cells 6 per cent, lymphocytes 3 per cent and monocytes 10 per cent. Reticulocytes constituted 1.2 per cent. Among the red cells there were many poikilocytes and microcytes. The icteric index was 8. The bleeding and clotting times were normal. Splenic puncture was suggested, but it was refused by the family physician, who desired the patient to have roentgen treatment to the spleen to shrink it. This was done, but after thirteen treatments of 200 roentgens, high voltage therapy was discontinued because of a low white cell count of 1,700, with 76 per cent polymorphonuclear leukocytes, 22 per cent lymphocytes and 2 per cent eosinophils. At this time the patient was discharged home to convalesce without a diagnosis having been made.

About two weeks later, on Jan. 22, 1938, the patient was readmitted for further study and treatment. The spleen had become enlarged in the interim since discharge and now reached almost to the iliac crests. The blood showed hemoglobin 59 per cent, red cells 3,000,000 and white cells 2,150; the differential count showed 84 per cent polymorphonuclear leukocytes (9 per cent band cells), 14 per cent lymphocytes, 2 per cent monocytes and 1 nucleated red cell per hundred white cells. On February 14 a splenectomy was done, no definite diagnosis having been reached preoperatively. The patient was given postoperatively a transfusion of 500 cc. of whole blood, and her convalescence was smooth. A check-up examination done on May 26 showed hemoglobin 89 per cent, red cells 6,000,000 and white cells 66,000; the differential count showed 40 per cent polymorphonuclears, 19 per cent band cells, 25 per cent lymphocytes, 10 per cent monocytes, 5 per cent eosinophils and 3 per cent basophils. There were 18 nucleated red cells and 2 erythroblasts per hundred white cells, urea nitrogen was 14.5, creatinine 0.5, uric acid 4.4, sugar 78, carbon dioxide 48.1, cholesterol 184 (free 59, or 32 per cent, ester 25), and in the galactose tolerance test all specimens were negative for galactose.

The Wassermann reaction was 2 plus on December 21 and negative on December 24. Total protein was 6.92, albumin 4.64 and globulin 2.28. Examination of the urine gave negative results.

Grossly the spleen was smooth, glistening, dark red brown and firm. On section the cut surface was similar in appearance to the liver, being homogeneously dark red, streaked here and there with lines of gray tissue and prominent channels.

Microscopically the spleen showed fibrous thickening of the capsule, trabeculae and reticulum. The malpighian corpuscles were reduced in number. There were megakaryocytes, myelocytes, plasma cells, eosinophils and a few polymorphonuclear leukocytes. There were no infarcts. A tentative diagnosis of Hodgkin's disease was made.

The patient had two subsequent admissions, July 17 to 19 and Oct. 22 to Nov. 7, 1938, both because of severe epistaxis, uncontrollable by packing at home. Transfusion was not necessary.

She was followed in the outpatient department from Nov. 10, 1938 until the present time. On Nov. 23, 1938 it was noted that the patient had a perforated septum. She continued to have epistaxis, which was treated locally with epinephrine and a thromboplastic substance. On Oct. 19, 1939 the patient complained of considerable itching of the legs. Roentgen treatment to the liver was given because of the diagnosis of Hodgkin's disease and to relieve itching. On Feb. 8, 1940 the patient complained of soreness of the tongue and bruising easily. By March severe glossitis had developed. The patient was given 100 mg. of nicotinic acid three times daily and two tablets of ferrous sulfate twice daily. On October 10 both glossitis and itching were somewhat improved. The skin was bronzed at that time. The liver was still enlarged, and the hemoglobin content was 15 Gm.

The patient was last seen on June 5, 1941. She had lost considerable weight, the liver was much enlarged and the skin was deeply bronzed. The blood showed hemoglobin 16 Gm., red cells 5,200,000 and white cells 41,000; the differential count showed polymorphonuclear leukocytes 51 per cent, of which 26 per cent were nonfilamented, lymphocytes 4 per cent, eosinophils 16 per cent, basophils 2 per cent, myelocytes 13 per cent and myeoblasts 4 per cent. The polymorphonuclear cells showed toxic granulations, and many abnormal platelets were seen.

CASE 4.—D. M., a German housewife aged 55, admitted to the hospital on Jan. 2, 1940, had noticed a swelling of the upper left portion of the abdomen five years before admission. The swelling was painless except for burning in this region on exertion. She had noted onset of weakness also at this time. The swelling had increased in size, and the patient had sought medical aid three years before admission. Since then she had had periodic courses of roentgen therapy, with a resulting decrease in the size of the mass, increased strength and amelioration of pain. The last roentgen treatment had been in May 1939, and she had entered the hospital for splenectomy, which was advised by her physician. There was no history of weight loss or jaundice. For an indefinite period she had had dyspnea and palpitation on climbing two flights of stairs. The family and past histories were not significant.

Physical examination showed her to be somewhat pale and only moderately ill. The upper teeth were missing, and the thyroid was of moderate size. There were pingueculae in the conjunctivas. The heart was moderately enlarged to the left. There was a rough reduplicated first sound heard loudest at the apex. The blood pressure was 185 systolic and 100 diastolic. There were many brown nevi on the skin of the abdomen. The flanks were bulging and were dull with a moderate fluid wave. The spleen was enlarged to 3 inches below the umbilicus. It was firm, smooth, nontender and movable. The liver was enlarged to 4 fingerbreadths below the right costal margin. There was also a tender, rounded bulge in the right costovertebral angle which seemed to be independent of the liver.

Laboratory studies showed the hemoglobin content to be 85 per cent, the red blood cell count 4,200,000 and the white cell count 7,500, with mature polymorphonuclear leukocytes 72 per cent, band cells 5 per cent, young forms 5 per cent, myelocytes 2 per cent, lymphocytes 6 per cent, monocytes 4 per cent, eosinophils 3 per cent and basophils 3 per cent. The red cells showed anisocytosis, poikilocytosis and basophilic stippling. A sternal puncture showed essentially normal marrow. The fragility test of the red cells showed normal resistance to saline solution. The bleeding and clotting times were normal.

Because of the mass in the right flank, intravenous urographic examination was performed, which showed bilateral diminished renal function. The pelves and calices were only faintly visualized.

On the eighth day after admission, splenectomy was performed after a preoperative diagnosis of Banti's syndrome. A biopsy specimen of the liver was obtained at the same time. Postoperatively the patient was given a transfusion of 500 cc. of whole blood. Save for mild pyelitis caused by Escherichia coli, which responded to sulfanilamide, the patient's convalescence was uneventful. She was discharged one month after operation.

Biopsy of the liver showed myeloid metaplasia. The weight of the spleen was 1,895 Gm. The capsule was thin and glistening, although in one area it was thickened and yellow gray. Several small nodules, of a consistency similar to that of the surrounding tissue, projected through the surface. On section the cut surface was smooth, firm, beefy and pink red, with fine streaks of gray white running through it. The follicles were not visualized. Large amounts of fluid blood ran from the cut surface.

Microscopically the spleen showed diffuse fibrosis and infiltration with small round cells, polymorphonuclear leukocytes, eosinophils and giant cells, these last being very numerous. The sinusoids were congested with blood. The malpighian corpuscles were absent.

Two months after discharge the patient reported that she had gained 10 pounds (4.5 Kg.) and felt well. She was seen again on June 9, five months postoperatively, at which time her general condition was good. She complained of pain around the stomach, and there was a large mass in the region of the liver, the nature of which was unknown. She was advised to enter the hospital for a check-up but did not do so.

On Jan. 29, 1941 the patient was readmitted to the hospital with swelling of the ankles. She was found to have cardiac enlargement with a mitral systolic murmur. The blood showed hemoglobin 13.5 Gm., red cells 4,200,000 and white cells 134,000, with 84 per cent polymorphonuclear neutrophil leukocytes, of which 57 per cent were nonfilamented, 6 per cent myelocytes, 7 per cent lymphocytes, 1 per cent monocytes and 2 per cent eosinophils and there were 6 nucleated red cells per hundred white cells. The sternal marrow showed fibrosis, otherwise hyperplasia of the remaining granular elements. She was given digitalis and discharged improved.

CASE 5.—M. T., a Negro aged 48, admitted to the City Hospital on Sept. 7, 1940, had been well until three months prior to admission, when dyspnea on exertion and a productive cough developed. The cough was associated with pain at the costovertebral angles. Two months before admission he noticed that both ankles were swollen. During the previous three weeks the dyspnea had increased gradually, so that at the time of admission he was unable to walk without discomfort. He did not complain of orthopnea or pain in the chest.

A family history was not given. He had had an attack of "rheumatism" twenty-four years before and had had nocturia, urinating two or three times a night, for an indefinite period. Otherwise his general health had been good until the onset of his present illness.

On physical examination the patient looked somewhat older than his stated age and was lying quietly in bed. The blood pressure was 124 systolic and 58 diastolic. The pupils reacted sluggishly to light. The mucous membranes were pale and the teeth carious. Examination of the heart and lungs gave negative results. On admission, neither the spleen nor the liver could be palpated. There was edema (3 plus) of the ankles. Rectal examination showed hemorrhoids. There was a questionable generalized cervical adenopathy.

About a week after admission the spleen became palpable and gradually increased in size until death. Two weeks after admission the liver was felt, and it gradually enlarged until it was 3 fingerbreadths below the costal margin.

Examination of the blood on the day of admission showed hemoglobin 25 per cent, red blood cells 1,600,000 and white cells 86,000, with 28 per cent polymorphonuclear leukocytes, 24 per cent stab cells, 4 per cent metamyelocytes, 20 per cent myelocytes, 3 per cent granuloblasts, 3 per cent progranulocytes A, 3 per cent eosinophils and 10 per cent lymphocytes. The red cells showed anisocytosis and poikilocytosis, together with some nucleation of red blood cells. A fragility test showed hemolysis of the red cells beginning in a 0.5 per cent salt solution and complete hemolysis in a 0.32 per cent salt solution. The icteric index varied between 16 and 35. On October 17 the reticulocyte count was 8.5 per cent. Gastric analysis showed no free

hydrochloric acid. The nonprotein nitrogen level was 30. A Wassermann test done at this time gave negative results.

Roentgen examination of the chest showed some scarring in the left apex. Examination of the bones showed no osteosclerosis. Retrograde pyelography and tests of the function of the kidneys gave evidence of bilateral chronic pyelonephritis and hydronephrosis.

Examination of the urine on repeated occasions showed the presence of erythrocytes and white cells but no casts.

The patient's course in the hospital was one of progressive asthenia, despite repeated transfusions which resulted only in slight improvement. Terminally, bilateral bronchopneumonia developed; he became irrational, had a uriniferous odor to his breath and died nine weeks after admission (five months after the onset of his illness).

Autopsy showed, in addition to lesions of myeloid metaplasia, acute and chronic pyelonephritis, acute bilateral bronchopneumonia and fibrinous pericarditis.

The spleen weighed 700 Gm. The capsule showed many areas of thickening, and the parenchyma was firm and fleshlike. The pulp could not be scraped at all. Microscopically it showed typical myeloid metaplasia and many megakaryocytes.

The liver and lymph nodes also showed many megakaryocytes. The bone marrow obtained was erythroblastic in type.

COMMENT

In not one of these cases was the diagnosis, either clinical or pathologic, correct. The clinical diagnoses were splenic anemia in 4 instances and leukemia in 1. The pathologic diagnosis of the condition of the excised spleen (the slides were sent to several reputable pathologists) was either atypical Hodgkin's disease or atypical leukemia.

On the strength of the clinical diagnosis splenectomy was performed, and because of the pathologic diagnosis radiation therapy was occasionally employed.

From a perusal of the case histories it is evident that both splenectomy and radiation therapy are harmful in this condition. The causes of the myeloid metaplasia are not known, but removal or depression of any of the foci seems to shorten the lives of the patients. This fact is illustrated not only in our cases but also in those of Jackson's series. He notes 2 cases in which death occurred shortly after irradiation. Three of his patients and 4 of ours did badly after splenectomy. Therefore, from a therapeutic point of view it is important to be on the lookout for this syndrome. It is easily confused with Banti's disease, hemolytic anemia, splenomegaly and atypical leukemia. Sternal puncture will rule out leukemia, since no leukemic infiltration has been observed in the marrow of these patients. Banti's disease and hemolytic anemia do not show both immature red and immature white cells in the peripheral blood. Normal red cell fragility and absence of spherocytes also distinguish agnogenic myeloid metaplasia from hemolytic anemia.

In dubious cases a prolonged period of observation is advisable, and, if necessary, a splenic biopsy can be taken through the peritoneoscope. The presence of myeloid metaplasia, many scattered foci of immature red and white blood cells and megakaryocytes definitely establishes the diagnosis of agnogenic myeloid metaplasia of the spleen.

CONCLUSIONS

1. Agnogenic myeloid metaplasia of the spleen is difficult to diagnose and must be differentiated from Banti's disease, hemolytic anemia and leukemia.

2. Splenectomy and irradiation are definitely contraindicated.

ETHER ANESTHESIA IN THE PRESENCE OF PULMONARY TUBERCULOSIS

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Great and sometimes dangerous efforts are made to avoid the use of ether anesthesia when surgery must be carried out on patients who happen to be suffering from tuberculosis; accordingly, it is important to examine the basis for the prejudice against the use of ether for tuberculous patients. As will be observed, this prejudice does not appear to be established on a secure foundation. We have therefore studied the results of using ether in operations on a carefully followed series of patients and have compared our results with those from other clinics.

Our wish to give ether an adequate trial was based on extensive observations, made in many general surgery clinics as well as our own, that ether is extraordinarily well tolerated by the cachectic patient and by the patient whose respiratory and circulatory systems may be grossly impaired.[1]

CURRENT BASIS FOR THE PREJUDICE AGAINST THE USE OF ETHER FOR PATIENTS WITH PULMONARY TUBERCULOSIS

Where the prejudice against ether originated is not clear, but the current basis for it can be found in many published opinions over the past twenty or thirty years.[2] These articles vividly describe the dangerous consequences of using ether anesthesia for tuberculous patients: It is plainly a bad agent to use, or so it is said, for "ether will dissolve the lipoid capsule surrounding the tubercle bacilli and allow them to be disseminated throughout the body." Liquid ether burns the skin, and so on; therefore "it must follow that the delicate mucosa of the airway will be dangerously irritated by the agent." (A considerable difference must exist in the effect produced by liquid ether and the concentration needed for full surgical anesthesia, namely 0.14 cc. of liquid ether per thousand cubic centi-

From the Anesthesia and Surgical Services of the Massachusetts General Hospital.

This is the third in a series of papers dealing with the problems of anesthesia for thoracic surgery: (Principles of Anesthesia for Lobectomy and Total Pneumonectomy, Acta med. Scandinav., supp **90:** 146, 1938, and the paper referred to in footnote 3).

1. In addition to the use of ether in a large number of patients at the Massachusetts General Hospital, with nearly all kinds and degrees of heart disease, ether has been our choice for patients suffering from many forms of chronic pulmonary disease as emphysema, chronic bronchitis, chronic lung abscess, bronchiectasis and cancer. In the surgical treatment of these, ether has been employed as the anesthetic agent of choice in 65 total pneumonectomies and 222 lobectomies with unusually good end results.[3]

2. These include, together with others:

Blumberg, N.: Ether Anesthesia and Tuberculosis with Report of Case, M. J. & Rec. **125:** 462 (April) 1927.

Eversole, U. H., and Overholt, R. H.: Anesthesia in Thoracic Surgery with Special Reference to Cyclopropane, J. Thoracic Surg. **5:** 510 (June) 1936.

Flemming, A. L.: Different Effects Produced by Exposing Tissues to Various Concentrations of Anesthetic Vapor, Brit. M. J. **2:** 921 (Nov. 11) 1922.

Frelich, E. B., and Ragino, O. B.: Ether in Tuberculosis, Illinois M. J. **56:** 67 (July) 1929.

Gwathmey, J. T.: Anesthesia, ed. 2, New York and London, Macmillan Company, 1925, p. 329.

Magill, I. W.: Anesthesia for Thoracoplasty in Pulmonary Tuberculosis, Lancet **1:** 295 (Feb. 8) 1930.

McDowall, R. J. S.: The Effect of Anesthetics on the Lungs, Brit. M. J. **1:** 61 (Jan. 13) 1923.

Shelley, L. W.: Anesthesia in Thoracic Surgery, Tubercle **5:** 13 (Oct.) 1923.

Zueblin, Ernst: Results of Ether Anesthesia on Suspected and Manifest Cases of Pulmonary Tuberculosis, Am. J. Surg. **34:** 44 (anesthesia supp.) (April) 1920.

Eastman.[6] Grandy.[7] Rogers.[10]

meters of air breathed.) Evidence that irritation from good ether anesthesia is probably not of morbid or mortal importance has been considered elsewhere.[3] This probability receives outstanding support in the observations of King [4] and others that an equal number of postoperative pulmonary complications are found in general surgery after ether, local or spinal anesthesia.

While opinions are divided at present concerning the advisability of using ether in operations on tuberculous patients, as shown in the following examples, there have been more to oppose than to approve or condone its use.[5] Following correspondence with about one hundred anesthetists, surgeons and internists, Eastman [6] found a great lack of unanimity of opinion as to the advisability of employing ether in the presence of pulmonary tuberculosis. Indeed, opinion varied from the conviction that ether would cure the tuberculosis to the belief that its use in operations on tuberculous patients is unqualifiedly foolhardy and, if administered to tuberculous patients, "sends them to their graves in less than six months." Unfortunately the statements of those questioned appeared to be made on the basis of memory and opinion rather than on a serious attempt to get at the facts through careful observation and record keeping.

Grandy [7] presents a vigorous condemnation of ether administered by inhalation to patients with pulmonary tuberculosis, and then at once speaks approvingly of ether by rectum. He concluded with the remark "I shall give only these 2 cases [of active tuberculosis] but these are enough to prove [!] that ether administered by rectum is entirely different from ether by inhalation." Among those who permit ether to be considered at all, this attitude is quite common. It ignores, of course, the well established fact that ether is almost entirely (above 90 per cent) excreted through the lungs. The alveolar air at once comes into near equilibrium with the ether tension in the blood, so that throughout maintenance and recovery the lungs are exposed to ether at the same tension, except for the brief induction period, as they would have been if the ether had entered through them rather than through the rectum. When ether is administered rectally, the difficulty of correlating the dose with the desired depth may in some cases be responsible for needlessly high concentrations reaching the lungs and acting for a longer time than when ether is given by inhalation.

While many papers have been found which deal with the use of ether in the presence of pulmonary tuberculosis, no report of careful case studies has been found. The articles referred to, apparently chiefly based on casual memory and opinion, seem to be the basis for the widespread belief as expressed in standard textbooks that ether is contraindicated or to be used with the greatest reluctance in the presence of tuberculosis.

EXPERIMENTAL STUDIES OF THE PAST CONCERNING THE USE OF ETHER IN THE PRESENCE OF PULMONARY TUBERCULOSIS

It is interesting to observe that whereas severe condemnation of ether for the tuberculous is common in the papers based on opinion, the three objective attempts to study the problem experimentally have come to quite another conclusion:

Corper [8] observed that ether to the point of light anesthesia daily for about a month did not increase the susceptibility of guinea pigs to a virulent human tuberculosis infection in comparison with controls.

Lawrason Brown and Petroff [9] studied three groups of tuberculous guinea pigs. In each of the first two groups, 4 pigs were exposed to ether anesthesia and 4 used as controls. In the third group 3 pigs were used in each test and control group. In the first group, two weeks following infection, ether anesthesia was administered at weekly intervals for seven weeks. The etherized group lived longer than the controls. The second group was treated the same as the first except that anesthesia was administered every four days. The etherized and control animals lived the same length of time. In the third group anesthesia was administered daily for fifteen days, and then the animals were killed. The tuberculosis was equally extensive in the test and the control groups. They conclude that "ether anesthesia, whether prolonged or of short duration, whether light or profound, exerts on tuberculous guinea pigs no injurious effect as noted in length of life or extent of disease."

Rogers [10] subjected 18 guinea pigs to tubercle bacillus infection; half received "complete ether anesthesia" daily for eleven days and half were used as controls. The duration (5 pigs) and extent (4 pigs) of the disease were identical in the two groups. He concluded that ether anesthesia has no effect on the disease process of tuberculosis.

Corper,[8] Brown and Petroff [9] and Rogers [10] have all reported that repeated ether anesthesia in tuberculous animals does not result in a more rapid spread of the disease process. Rogers concludes that the "rapid spread of the disease [which] often followed operations on the tuberculous under ether anesthesia" is due to mechanical factors. He suggests that spread of the disease is due to "aspiration from the apical lesion, usually a cavity, to the larger areas of the lung substance, causing aspiration bronchopneumonia and after a few months death." Any factors such as labored respiration or excessive body movements aid in this aspirating process, according to him. He states further that "ether anesthesia not only causes labored respiration but increases the secretions diluting the infectious germ laden sputum and in this way causes a general spreading of the disease germs." He goes on to say that, "in the laboratory animal, the disease is anatomically different, inasmuch as the chronic ulcerative form is not present, but more of a solitary tubercle formation without ulceration, hence the aspirating of infectious material does not occur."

Whether or not Roger's explanation is correct, it is interesting that the only objective examinations made of this problem, the experimental studies, fail to provide any grounds for discrediting the employment of ether for the tuberculous patient. While the experimental studies leave much to be desired in their attack on the problem, it is probably true, as suggested by Rogers,

3. Beecher, H. K.: Some Controversial Matters of Anesthesia for Thoracic Surgery, J. Thoracic Surg. **10:** 202 (Dec.) 1940.
4. King, D. S.: Postoperative Pulmonary Complications: The Part Played by Anesthesia, Anesth. & Analg. **12:** 243-248 (Nov.-Dec.) 1933.
5. Savage, W. E.: The Treatment of Tuberculosis by Ether, Ohio State M. J. **14:** 480 (July) 1917; The Treatment of Tuberculous Peritonitis by Ether, Anesth. & Analg. **7:** 137 (May-June) 1928, and, with the exception of Rogers,[10] the references cited in note 2.
6. Eastman, J. R.: Anesthesia in the Tuberculous, Am. Rev. Tuberc. **9:** 276 (May) 1924.
7. Grandy, C. R.: Ether Anesthesia in Cases of Pulmonary Tuberculosis, Am. Rev. Tuberc. **16:** 262 (Sept.) 1927.
8. Corper, H. J.: Attempts to Reduce the Resistance of the Guinea Pig to Tuberculosis by Means of Various Agents (Including Ether and Chloroform), Am. Rev. Tuberc. **2:** 587 (Dec.) 1918.
9. Brown, Lawrason, and Petroff, S. A.: The Influence of Anesthesia on Experimental Tuberculosis in Guinea Pigs, Tr. Nat. A. Prev. Tuberc. **15:** 292, 1919.
10. Rogers, J. B.: Studies in Effects of Nitrous Oxide-Oxygen Anesthesia on Animals Infected with Tuberculosis Through the Respiratory Tract, Am. J. Surg. **35:** 44 (anesthesia supp.) (April) 1921.

that the tuberculosis process is sufficiently different in guinea pigs, ulcerative pulmonary lesions and cavities so rare in them, that the problem at hand cannot be settled by such an approach. With the possible exception of studies in monkeys it is questionable whether any animal experimental work would be of further

TABLE 1.—*Type of Operation and Duration of Anesthesia in 147 Cases*

Operations		Average Duration of Anesthesia *
First stage	139	2 hours and 8 minutes
Second stage	106	1 hour and 26 minutes
Third stage	15	1 hour and 22 minutes
Total	260	

* "Duration of anesthesia" was taken as the period from the beginning of induction until the operation was completed.

value in giving information on the problem at hand; certainly any attempts to get more help from animals would have to be very extensive. However, the three independent studies referred to, having arrived at a common conclusion, need not be passed by entirely. This negative evidence thrice obtained is of some value. Evidently the belief that the lipid solvent action of ether is a danger is on a less secure basis than has been supposed. It is apparent that, even in the highly susceptible guinea pig, ether anesthesia does not aggravate the disease process. This point at least can reasonably enter to a limited degree into our consideration.

While statements based on opinion appear to have served as the basis for the numerous strictures against ether in the tuberculous, so many men have been of this view that one cannot lightly dismiss their statements. A point worth noting here is that nearly all, if not all, of the statements referred to were based on open cone anesthesia, not modern, closed anesthesia. Surely open cone anesthesia is objectionable in these cases (and in many others) for several reasons: The vapors breathed are cold. One must deal not only with possible irritation due to the ether itself but also with that due to chilling the lungs. With less than expert cone administration of ether, the concentration of the agent breathed will at times be very much greater than needed and consequently more irritating than necessary. In the great majority of cases, cones are used in a manner that serves to increase considerably the dead space of the airway, with an objectionable elevation of the carbon dioxide tension and a lowering of the oxygen in the air breathed. Often the so-called open cone is nothing short of an asphyxiating tool.

With the simple modern equipment at hand, it is easy to avoid these difficulties encountered with the open cone. We believed that ether employed in modern closed anesthesia with the carbon dioxide absorption technic is worthy of trial and reevaluation in tuberculosis, for, as pointed out earlier, ether has many desirable qualities for the very sick. Ether administered in a closed system can hardly be compared with the agent when it is used by the open drop method.

Accordingly, we have carefully studied for a period of more than five years a series of patients who received "closed" ether anesthesia, notwithstanding their pulmonary tuberculosis. Our major purpose in this paper is to report that experience.

USE OF ETHER IN THE PRESENCE OF PULMONARY TUBERCULOSIS AT THE MASSACHUSETTS GENERAL HOSPITAL

We began to use ether routinely as the anesthesia of choice for thoracoplasty in patients with pulmonary tuberculosis in October 1935. This beginning was made under the direction of Dr. H. H. Bradshaw. The present study concerns consecutive patients treated from that date through 1940: 229 tuberculosis patients received ether anesthesia for four hundred and four thoracoplasties during this period. While the majority of the patients came from the Rutland Sanatorium, a number of other sanatoriums participated. Since more precise follow-up information was available concerning the Rutland patients, we decided to limit our study to this group: 147 patients who underwent two hundred and sixty thoracoplasties under ether anesthesia.

Details concerning choice of patient for thoracoplasty, surgical indications and procedures and similar material are recorded in a recent paper from this clinic by Adams and Dufault.[11] The routine premedication consists of morphine sulfate ⅙ grain (0.01 Gm.) and atropine 1/100 grain (0.00065 Gm.) administered subcutaneously one-half hour before operation. Frequently, soluble pentobarbital 1½ grains (0.1 Gm.) is given by mouth one hour before operation. Patients are placed in position for operation before anesthesia is induced. During induction, care is taken to prevent straining and coughing. The choice of operating time is the afternoon, following elimination of the morning sputum. Anesthesia is administered by means of a closed system apparatus with carbon dioxide absorption (never open cone for these patients). Following a brief nitrous oxide-oxygen induction, with care to avoid anoxemia, ether anesthesia is administered with a high percentage of oxygen. Although intratracheal tubes are used with great frequency in this hospital and are always used in open pleura operations, we rarely use them in the presence of pulmonary tuberculosis. They are used in this case only when the sputum is unusually abundant. We are reluctant to use them in most cases of tuberculosis, for possibly new loci of tuberculous infection might develop in areas of slight trauma to the airway. During operation the patient is maintained in a slight Trendelenburg position.

TABLE 2.—*Results* of Thoracoplasties (Including Tuberculous Empyema)*

Patients		Number	Per Cent
Apparently cured		75+	59.5+
Arrested		11+	8.7+
Apparently arrested		2+	1.6+
Quiescent		18	14.3
Unimproved		1	0.8
Worse		1	0.8
Dead		16	12.7
Early†	8		
Late	8		
Unknown		3	2.4
Total in this group		126	
Total well		88+	69.8+

The 21 patients operated on in 1940 have not been included in this end result table, since a one year follow-up is not adequate for indicating disposition; yet all of the operative complications as anoxia and shock, pneumonia and atelectasis as well as spread occurring in the 1940 patients have been included in the complications; see table 3.

* According to the National Tuberculosis Association's method of classification.

† That is, within the customarily stated but purely arbitrary two month period following operation.

With termination of the study reported here, at the end of December 1940, all patients will have been

11. Adams, Ralph, and Dufault, Paul: Surgery in Pulmonary Tuberculosis, J. Thoracic Surg. **11**: 43 (Oct.) 1941.

followed for at least one year after their last anesthesia and operation. It would seem reasonable to suppose that damage possibly caused by the anesthesia would become evident within that time. The "end result" data of table 2 run only until the end of 1939; thus these patients have all been followed for at least two years.

It is unquestionably important in computing end result data in a study of this kind to consider the number of patients studied rather than the numbers of anesthesias and operations; nevertheless, in order to show distribution of type of operation, and frequency and duration of repeated anesthesias, the number of operations has occasionally been considered, as in table 1.

As shown by the study of Adams and Dufault [11] the patients coming from the Rutland Sanatorium to the Massachusetts General Hospital for treatment of their pulmonary tuberculosis gave the following distribution of conditions requiring surgery: cavernous disease, 87 per cent; pulmonary tuberculosis and tuberculous empyema, 5 per cent; pulmonary tuberculosis and mixed empyema, 5 per cent; unstable fibrotic disease without demonstrable cavitation, 3 per cent; early bronchial disease, 1 per cent. Our material deals with consecutive cases from the Rutland Sanatorium; those having tuberculous empyema as well as other unfavorable complications are of course included. The composition of the surgical teams changed frequently. The surgeons varied from members of the house staff to the chief of service.

TABLE 3.—*Postoperative Complications*

(Total number of patients, 147; total number of operations, 260)

Complications	Number	Per Cent Based on Number of Patients	Per Cent Based on Number of Operations
Anoxemia and shock	3	2.0	1.2
Pneumonia	4	2.7	1.5
Atelectasis	4	2.7	1.5
Ipsilateral spread	5	3.4	
Contralateral spread	3	2.0	

This table, based on the "early" complications (within two months), does not include wound infection (5 cases), late secondary wound hemorrhage (1 case) or torn pleura (1 case), since these are clearly unrelated to anesthesia, although these are all set down in the brief case summaries.

COMPLICATIONS AND DEATHS

Of the 147 patients (two hundred and sixty anesthesias and operations) the early complications and deaths are summarized here. This "early" group covers the customarily stated but purely arbitrary period of two months following operation. The "late" complications and deaths are subsequently grouped together.

EARLY

D. P. D., 1935. A man aged 24 died of ipsilateral, acute bronchiogenic spread of tuberculosis nineteen days after the third stage operation.

J. J. O'L., 1935. A man aged 20 died two days after first stage thoracoplasty and apicolysis of shock and anoxemia.

T. H., 1936. A man aged 30 died five weeks after first stage thoracoplasty of anoxemia, atelectasis, hemoptysis and ipsilateral spread of disease.

W. T., 1936. A man aged 26 developed bronchopneumonia two days after first stage thoracoplasty. This completely cleared within two months. After a second stage operation he is now well and working.

R. L., 1936. A man aged 36 was cyanotic following a first stage thoracoplasty. He was completely relieved by circulatory stimulants and oxygen. Surgical shock followed a second stage operation; this was combated successfully with intravenous saline solution.

S. P., 1937. A woman aged 36 died three days after a second first stage thoracoplasty with apicolysis (bilateral first stages and one second stage) of hemolytic streptococcus wound infection.

J. W., 1937. A man aged 46 developed bronchopneumonia four days after a second stage thoracoplasty; this cleared within three weeks.

R. K., 1937. A man aged 48 died five days after a second stage operation of shock and prolonged circulatory failure.

M. MacF., 1937. A woman aged 37 died five days after a third stage thoracoplasty of atelectasis and anoxia.

E. McC., 1937. A man aged 25 died eight days after a second stage thoracoplasty of wound infection.

A. P., 1938. A man aged 27 died one month after a third stage thoracoplasty of major hemorrhage in wound.

J. T. H., 1938. A man aged 46 showed ipsilateral spread of disease within three weeks of a first stage thoracoplasty. He died one year later of progression of the disease.

C. G., 1938. A man aged 41 developed atelectasis, after a first stage thoracoplasty, the day of operation. This persisted for six days, then cleared.

P. Q., 1938. A woman aged 37 with bilateral cavitation showed exacerbation of the process contralateral to operation within two weeks of a first stage thoracoplasty.

M. E. H., 1938. A woman aged 32 suffered a torn pleura during a second stage thoracoplasty with resulting pneumothorax.

G. C., 1938. A man aged 47 immediately after a first stage thoracoplasty developed bronchopneumonia which persisted for twenty-three days. This was followed by ipsilateral spread of the disease and death one year later.

W. E. G., 1938. A man aged 30 showed, twelve days after a first stage thoracoplasty, signs of a contralateral spread. These cleared in four months and a second stage operation was performed.

R. P., 1939. A man aged 41 with bilateral cavernous tuberculosis developed bilateral bronchopneumonia two days after a first stage thoracoplasty. This cleared in two weeks.

J. K., 1939. A man aged 23 had wound infection and ipsilateral spread within a week after a first stage thoracoplasty.

W. J. F., 1940.[12] A man aged 44 with bilateral tuberculosis showed major wound infection and contralateral spread of tuberculosis following a first stage thoracoplasty. Death was caused by the wound infection and progressive cavernous tuberculosis two months after operation.

R. U., 1940.[12] A man aged 34 developed atelectasis three days after a first stage thoracoplasty. The reaction required twenty-eight days to subside. Later a second stage operation was performed without unusual incident.

J. D., 1940.[12] A man aged 27 died thirteen days after a second stage operation, of wound infection.

LATE

G. B., 1935. A woman aged 26 died of progression of tuberculosis one year after a first stage thoracoplasty.

A. F. J., 1935. A man aged 36 died of progression of tuberculosis eight months after a first stage thoracoplasty.

J. F. O'C., 1936. A man aged 32 died of intestinal obstruction caused by tuberculosis two years after a second stage thoracoplasty.

M. F., 1937. A man aged 26 died of progression of pulmonary tuberculosis and extrapulmonary tuberculosis nine months after a third stage thoracoplasty.

J. W., 1938. A man aged 47 died of progression of his disease, six months after a second stage thoracoplasty.

J. T. H., 1938. (Included in preceding "early" group, which see, since it showed early spread of disease but was classified as a late death.)

G. C., 1938. (Included in preceding "early" group because of early complications. Classified as a late death.)

W. J., 1938. A man aged 31 died of progression of disease and wound infection eight months after a first stage thoracoplasty.

12. The 1940 data are too recent to include in table 2, which deals only with material through 1939. However, the complications of 1940 are included in table 3.

COMPARISON OF OUR RESULTS WITH THOSE FROM VARIOUS CLINICS

In our series of 126 cases of thoracoplasty for tuberculosis from 1935 through 1939 under ether anesthesia there have been eight early deaths (6.3 per cent), that is, within the customarily stated but purely arbitrary period of two months after operation, and eight later deaths (6.3 per cent) for a total death rate of 12.7 per cent from tuberculosis in any form and from causes directly or indirectly connected with the operation: 59.5 per cent of the 126 cases are apparently cured, 8.7 per cent arrested, 1.6 per cent apparently arrested and 14.3 per cent quiescent.

Haight and Alexander [13] reported a death rate of 5.6 per cent in 178 cases between 1934 and 1937 from causes directly or indirectly connected with operation, and a total death rate of 6.1 per cent. In another group of 119 cases, probably including many of the foregoing, they had 83.1 per cent apparently arrested cases from two and one-half months to two years after operation. At the time these data were compiled, nitrous oxide was chiefly favored by Alexander as the anesthetic agent (pp. 443, 444, 448).

Skinner, Macpherson and Allen,[14] report 3.2 per cent early deaths and 4.8 per cent total tuberculous deaths in a series of 126 cases from 1936 to 1940. The anesthesia which they used (personal communication) was avertin with amylene hydrate plus nitrous oxide in nearly all cases. Cyclopropane was used in a few cases.

Finney [15] had an operative mortality of 5.7 per cent and a total mortality of 18.2 per cent in a group of 104 cases between 1932 and 1940, with arrest of disease in 42.3 per cent and apparent arrest in 20.2 per cent. Avertin with amylene hydrate and nitrous oxide-oxygen were used in the earlier cases and cyclopropane in the later ones.

Meltzer,[16] using local anesthesia exclusively, reported that he obtained arrest of disease in 32 per cent and apparent arrest in 31.4 per cent of 181 patients from 1936 to 1941, with an operative mortality of 1.6 per cent and a total mortality of 4.4 per cent.

Aufses [17] had an operative death rate of 7 per cent and a total death rate of 11 per cent in 90 cases between 1935 and 1940, using nitrous oxide-oxygen, avertin with amylene hydrate and cyclopropane, and the disease of 71 per cent of his cases was arrested.

Diffenbach and Crecca,[18] using evipal and nitrous oxide-oxygen, reported 100 cases in which operation was performed during the period 1936 to 1938, with an early mortality of 2 per cent, a total mortality of 13 per cent and arrest of disease in 71 per cent.

The averages for these seven groups of cases are shown in table 4. Except for the figures from Haight and Alexander, the data are the most recent published, representing the authors taking part in the Symposium on Results from Thoracoplasty at the twenty-fourth annual meeting of the American Association for Thoracic Surgery, Toronto, Canada, in June 1941.

TABLE 4.—*Averages in Seven Groups of Cases* *

Authors	Major Anesthetic Agent	Cases	Early Death Rate	Total Death Rate	Apparently Arrested, Arrested and Apparently Cured	
Aufses.....	Nitrous oxide.....	90	7.0	11.0	71.0	
Diffenbach and Crecca	Evipal plus nitrous oxide	100	2.0	13.0	71.0	
Finney.....	Early, avertin with amylene hydrate and nitrous oxide; recently, cyclopropane	104	5.7	18.2	62.5	
Beecher and Adams	Ether.....	126	6.3	12.7	69.8	84.1†
Skinner et al.	Avertin with amylene hydrate and nitrous oxide; a few, cyclopropane	126	3.2	4.8	80.0	
Haight and Alexander	Nitrous oxide.....	178	5.6	6.1	83.1	
Meltzer.....	Local.....	181	1.6	4.4	63.4	
Total patients.....		905				
Average (with standard deviations)		129	4.5±0.9	10.0±1.9	71.5± 3.0	

* It is impossible to determine from some of these series whether or not patients having empyema were included. The inclusion of empyema cases interferes greatly with good average end result figures. All empyema cases that we encountered in the consecutive cases studied were included in our data.

† If we include our quiescent cases here, as some writers appear to have done, 69.8 per cent becomes 84.1 per cent. It was not possible to break down the data from the several clinics presented here as they should be according to the National Tuberculosis Association classification; namely, as apparently cured, arrested, apparently arrested and quiescent. Our figures for these respective groups are shown in table 2.

It is apparent that the results in our cases have fallen near the average in the several categories. On the basis of these comparative data, no outstanding virtue can be claimed for one anesthetic agent nor particular hazard charged against another, as far as the results in these seven series go. Certainly it is true here as elsewhere that the anesthetist is of more importance than the anesthetic agent employed. To let one's conclusions rest here, however, implies a rather restricted view of the matter. It seems to be true that any one of two or three agents can safely be employed in the presence of pulmonary tuberculosis without aggravating this disease process. One might assume therefore that, if a well trained anesthetist is available, these two or three agents are all equally desirable. We doubt the validity of such an assumption, for it implies that the absolute death rate is the same for all of these agents. While it is admittedly difficult if not impossible to get precise information on this subject, enough evidence is available to indicate that wide differences exist between the death rates of the common anesthetic agents. Since this is the case it seems wiser to choose the agent which allows two important things: (1) the lowest death rate when large masses of data are considered, in other words jeopardizes the patient the least, and (2) permits the surgeon the greatest freedom. The low death rate of ether has been established in general surgery from its use in very sick patients in many hundreds of thousands of cases. The death rates of some other common general anesthetic agents appear to be at least twice as high as that of ether. In addition to these matters, the following should be considered: When the anesthesia is to be chosen for thoracoplasty, we believe it to be of great importance to choose ether, for on the basis of a considerable experience with patients who undergo all kinds of thoracic surgery it is our observation that many of the obvious as well as less apparent difficulties encountered during these operations are caused by reflex phenomena medi-

13. Alexander, John: The Collapse Therapy of Pulmonary Tuberculosis, Springfield, Ill., Charles C. Thomas, 1937, pp. 562, 564.
14. Skinner, G. F.; Macpherson, Lachlan, and Allen, Irene: Thoracoplasty for Tuberculosis, J. Thoracic Surg. **11**: 54 (Oct.) 1941.
15. Finney, G. G.: Analysis of 104 Cases of Thoracoplasty for Pulmonary Tuberculosis, J. Thoracic Surg. **11**: 76 (Oct.) 1941.
16. Meltzer, Herbert: Results of Thoracoplasty, J. Thoracic Surg. **11**: 84 (Oct.) 1941.
17. Aufses, A. H.: Results in Ninety Consecutive Thoracoplasties for Pulmonary Tuberculosis, J. Thoracic Surg. **11**: 98 (Oct.) 1941.
18. Diffenbach, R. H., and Crecca, A. D.: Analysis of 100 Consecutive Cases of Thoracoplasty with No Operative Mortality, J. Thoracic Surg. **11**: 65 (Oct.) 1941.

ated through the vagi. The depression of vagal activity accomplished by ether is of real importance in thoracic surgery. We have reached this conclusion on the basis of data obtained in the clinic as well as in the anesthesia laboratory. In this regard ether exceeds in value all other agents studied to the present time.

Since the choice of closed ether anesthesia presents no hazard to the tuberculosis process, as far as we have been able to determine, it appears to us to be the best choice for the reasons that have been mentioned, for use in operations on patients who are suffering from tuberculosis whenever they require general anesthesia, whether this is for surgical treatment of pulmonary tuberculosis or for surgical treatment of other lesions.

SUMMARY

A prejudice exists against the use of ether anesthesia for operations on tuberculous patients. Where this originated is uncertain, but the current basis for it can be found in numerous published statements. On examination, these statements do not appear to be founded on study and careful record keeping; casual opinion appears to have served as the basis for many of the statements voiced against ether. Three groups of workers have in the past attacked the problem experimentally. Not one was able to substantiate the prejudice against the use of ether anesthesia for operations on the tuberculous. Most of the articles which apparently serve as the basis for the current prejudice against ether were written from one to three decades ago and were based on observations of "open cone" or "open drop" ether administration. It is probable that some of the secondary results of the use of this technic are undesirable in the presence of pulmonary tuberculosis as elsewhere.

Since the prejudice against the use of ether anesthesia for operations on the tuberculous does not appear to be based on a secure foundation and since, as far as we have been able to find, no extensive clinical study of this matter has been carried out, we have for more than five years been using closed ether anesthesia (with carbon dioxide absorption) in operations on consecutive patients undergoing surgical treatment of their pulmonary tuberculosis. Our data include all cases, favorable and unfavorable. The surgical teams were constantly changing, the surgeons varying from members of the house staff to the chief of service. Notwithstanding these facts, our results for more than five years are such as to compare favorably with those from other clinics where ether is used either not at all or rarely.

In our opinion, the anesthetic agent is not important in these cases as long as it permits the use of a plentiful supply of oxygen and allows the surgeon to carry out a deliberate, unhampered and unhurried operation, provided the patient is not jeopardized by toxic action of the anesthetic. It is important to choose an anesthetic agent which depresses vagal activity when thoracic surgery is contemplated. Ether excels other agents studied in this regard. While not enough data have been collected to permit final statement, several of the newer anesthetic agents appear to have a death rate in general surgery two or three times higher than is the case with ether. The excellent tolerance of the very sick patient for ether anesthesia as well as the low death rate attributable to this agent are well established. After five years of study we can see no reason to abandon the use of ether in operations on the tuberculous patient because of the presence of tuberculosis.

UNTOWARD EFFECTS OF PHENYTOIN SODIUM IN EPILEPSY

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Merritt and Putnam [1] found that while phenytoin sodium (sodium diphenyl hydantoinate, or dilantin sodium) was effective in protecting animals from electrically induced convulsions it produced little sedative effect. The effectiveness of this drug was then determined by them [2] in a group of 200 patients who had been having frequent convulsive seizures for many years and who had obtained little or no benefit from the usually accepted treatment. Certain toxic effects were observed, among them dermatitis, nonthrombopenic purpura, tremors, ataxia and dizziness.

Although Fetterman [3] reported that phenytoin sodium had a high degree of therapeutic value, he observed disquieting side actions such as itching, a cutaneous rash, swelling of the gums, tremors and ataxia, blurring of vision, loss of taste and dysesthesia in the mouth, restlessness, insomnia, irritability, paranoid state, anorexia, gastric distress and loss of weight. A study of the table published by Fetterman shows that 23 of 28 patients, or 82 per cent, had some toxic effects. Epistaxis was mentioned by Frost [4] as a complication. Kimball [5] reported hyperplasia of the gums. Merritt and Putnam [6] later mentioned diplopia with nystagmus, drowsiness, headache, psychotic reaction, hypertrophy of the gums and slight secondary anemia in a small percentage of patients. Blair, Bailey and McGregor [7] reported the side effects of giddiness, tremor, ataxia, blurring of vision, slight nausea, delusions, hallucinations, prolonged confusion, clonic spasms, agitation, mental depression and reactivation of suicidal tendencies in an unspecified number of their 75 institutionalized patients treated with phenytoin sodium. Toxic reactions in some degree occurred in the majority (73 per cent) of Pratt's 52 cases.[8] In addition to the usual side actions such as subjective tremulousness and a feeling of apprehension and tension, tremors, burning sensation in the eyes, blurring of vision, diplopia, dizziness, ataxia, nausea and vomiting, 5 patients had psychotic states. Blair [9] reported a case of hemiplegia developing as a complication of treatment with phenytoin sodium. He [10] later reported the results of treatment of 36 institutionalized patients with phenytoin sodium. Twenty-one, or 58.3 per cent, developed severe nervous toxic symptoms. Of particularly ominous nature seemed

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1. Merritt, H. H., and Putnam, T. J.: A New Series of Anticonvulsant Drugs Tested by Experiments on Animals, Arch. Neurol. & Psychiat. **39:** 1003 (May) 1938.
2. Merritt, H. H., and Putnam, T. J.: Sodium Diphenyl Hydantoinate in the Treatment of Convulsive Disorders, J. A. M. A. **111:** 1068 (Sept. 17) 1938.
3. Fetterman, J. L.: Dilantin Sodium Therapy in Epilepsy, J. A. M. A. **114:** 396 (Feb. 3) 1940.
4. Frost, I.: Sodium Diphenyl Hydantoinate in Treatment of Severe Cases of Epilepsy, J. Ment. Sc. **85:** 976 (Sept.) 1939.
5. Kimball, O. P.: The Treatment of Epilepsy with Sodium Diphenyl Hydantoinate, J. A. M. A. **112:** 1244 (April 1) 1939.
6. Merritt, H. H., and Putnam, T. J.: Sodium Diphenyl Hydantoinate in Treatment of Convulsive Seizures: Toxic Symptoms and Their Prevention, Arch. Neurol. & Psychiat. **42:** 1053 (Dec.) 1939.
7. Blair, Donald; Bailey, K. C., and McGregor, J. S.: Treatment of Epilepsy with Epanutin, Lancet **2:** 363 (Aug. 12) 1939.
8. Pratt, C. H.: Sodium Diphenyl Hydantoinate and Its Combination with Phenobarbital in the Treatment of Epilepsy, J. Ment. Sc. **85:** 986 (Sept.) 1939.
9. Blair, Donald: Hemiplegia Complicating Sodium Diphenyl Hydantoinate Therapy in Epilepsy, Lancet **1:** 269 (Feb. 10) 1940.
10. Blair, Donald: The Modern Treatment of Epilepsy, J. Ment. Sc. **86:** 888 (Sept.) 1940.

psychosomatic delusions, revival of such psychotic symptoms as severe depressions and the like. Loss of weight was frequent, occurring in 15 out of 20 patients. Eosinophilia (between 4 and 12 per cent) occurred in a few cases and in 2 cases a reduction in red blood cells occurred. Pratt [8] found a mild albuminuria in some cases. McCartan and Carson [11] reported that toxic symptoms developed in 40 per cent of their 20 cases. In some of their cases a decided twitching of the orbicularis oris preceded by two to three weeks the development of ataxia. In every case there was a slight, progressive diminution of the red cell count. There was a tendency to a lowering of the white cell count due to a fall of granulocytes. In 13 cases (65 per cent) there was a rise in the number of eosinophil cells.

Williamson [12] reported severe toxic effects of phenytoin sodium in mentally defective patients with epilepsy. He said that these toxic reactions were clinically identifiable with a state closely resembling nirvanol poisoning. Of the toxic reactions, Williamson noted widespread furunculosis in 1 case, edema of the face in 2 cases, an urticarial wheal along the mucocutaneous margin of the lips in 1 case and gingival hyperplasia with bleeding in 1. There was 1 case in which there was a persistently low blood urea and 2 cases in which there was hematoporphyrinuria. There were 4 deaths among the 20 patients treated, or a mortality of 20 per cent. In the cases terminating fatally oliguria was the rule. An intermittent temperature of 100 to 102 F. appeared late. In 1 case it rose to 106 F. forty-eight hours before death, while in other cases the terminal temperature was subnormal. Death was due to bronchopneumonia in 1 case and to status epilepticus in 3. Status epilepticus set in in the 3 cases after phenytoin sodium therapy had been administered for one-half month, one-half month and two and one-half months respectively. In 1 case the treatment was discontinued after three months because a tendency to status epilepticus began.

Williams [13] reported that 2 patients died in status epilepticus while on phenytoin sodium and bromides. Phenytoin sodium had at first obviously had a good therapeutic effect, yet status epilepticus later developed while the patients were under full treatment with the drug. Status developed in 1 case after a remission of five weeks while on treatment and in the other after a remission of two months while on treatment. He also found that toxic symptoms arose in 36 per cent of his 83 patients. The toxic complications involving the nervous system included bifrontal headaches, lethargy, bilateral ptosis, blurring of vision, diplopia, ataxia, tremor and nystagmus in all directions. Behavior disturbances also occurred which might be attributed to the toxic effects of phenytoin sodium.

Blair [10] reported 4 deaths but could not definitely prove the association of death to the use of phenytoin sodium. In 1 case phenytoin sodium was withdrawn long before death. One death was due to cardiac involvement in a patient with known cardiovascular disease. In the other 2 cases, however, postmortem examination showed myocardiac damage, and we believe that phenytoin sodium had a toxic influence on the myocardium leading to a fatal termination.

Blair [10] also noted in 4 cases a noticeable exacerbation of spells following a long period free from spells due to phenytoin sodium therapy. An increase of phenytoin sodium dosage led to an increase of seizures. Reduction of the dose led to a reduction of the seizures.

Coope and Burrows [14] had 2 fatalities due to bronchopneumonia following an acute exacerbation of seizures: a woman aged 31 had a series of six severe major attacks after three weeks on phenytoin sodium therapy and three seizures the next day. Phenytoin sodium was discontinued and she was given bromides, a chloral derivative and phenobarbital, but she had fifteen attacks the following day. Three days later she died of bronchopneumonia. The other patient who died was a youth aged 18 who after two weeks on phenytoin sodium therapy had two seizures. After two more weeks he had two, four and nineteen spells on successive days, his temperature rose to 105 F. and he died of a disseminated bronchopneumonia.

Kimball and Horan [15] reported repeated attacks of gastrointestinal irritability together with unusual hyperplasia of the gums. Mandelbaum and Kane [16] reported a case in which there was pyrexia, dermatitis exfoliativa and considerable enlargement of the liver and spleen. The serum phosphatase value was found to be increased to 15.4 mg. per hundred cubic centimeters. Phenytoin sodium was given in 1½ grain (0.1 Gm.) capsules two or three times a day. The rash was first noted after thirty-nine capsules had been taken and the more severe toxic effects occurred after seventy-nine capsules had been ingested.

Aring and Rosenbaum [17] reported that a young man on three occasions ingested 60, 90½ and 105 grains (4, 6 and 7 Gm.) of phenytoin sodium over a period of minutes, six hours and ten hours respectively. The chief resulting symptoms were exhilaration, light headedness, dizziness, nausea and vomiting, headache, staggering, diplopia, nystagmus, difficulty in converging the eyes, pupillary abnormalities, ataxia, tremor and changes in reflexes. Of all these signs, nystagmus persisted the longest and was present for eight days on the last occasion.

OUR OBSERVATIONS

Forty-four patients with epilepsy who had previously been treated with bromides or phenobarbital for at least six months were each given from 0.3 to 0.6 Gm. of phenytoin sodium daily. Four of these patients were from the private practice of Dr. L. J. Pollock. The remainder were from the Epilepsy Clinic of Northwestern University Medical School. Phenytoin sodium was administered according to the method advised by Merritt and Putnam. The previous medication was gradually withdrawn as phenytoin sodium was overlapped and finally substituted. Treatment was begun on 20 patients in April 1939. As patients were found suitable for this treatment they were added shortly after that date until a total of 44 was reached. However, at the present time only 7 patients remain on active treatment with phenytoin sodium.

The reasons for discontinuing the medication after varying lengths of time from two weeks to several months were as follows: It was discontinued in 3 cases because of an increased frequency of spells, in 6 because of a severe ataxia, in 1 because of a severe gastrointestinal disorder, in 7 because there was no reduction in the number of seizures, in 4 because psychotic

11. McCartan, W., and Carson, J.: The Uses of Sodium Diphenyl Hydantoinate, J. Ment. Sc. **85**: 965 (Sept.) 1939.
12. Williamson, B. A. M.: Severe Toxic Effects of Sodium Diphenyl Hydantoinate in Mentally Defective Epileptics, J. Ment. Sc. **86**: 981 (Sept.) 1940.
13. Williams, Denis: Treatment of Epilepsy with Sodium Diphenyl Hydantoinate, Lancet **2**: 678 (Sept. 23) 1939.
14. Coope, Robert, and Burrows, R. G. R.: Treatment of Epilepsy with Sodium Diphenyl Hydantoinate, Lancet **1**: 490 (March 16) 1940.
15. Kimball, O. P., and Horan, T. N.: The Use of Dilantin in the Treatment of Epilepsy, Ann. Int. Med. **13**: 787 (Nov.) 1939.
16. Mandelbaum, Harry, and Kane, L. J.: Dilantin Poisoning, Arch. Neurol. & Psychiat. **45**: 769 (May) 1941.
17. Aring, C. D., and Rosenbaum, Milton: Ingestion of Large Doses of Dilantin Sodium, Arch. Neurol. & Psychiat. **45**: 265 (Feb.) 1941.

behavior developed, in 4 because of the development of an encephalopathy, in 3 because there were electrocardiographic changes and subjective complaints of precordial distress, in 5 because of irritability and apprehensiveness and the refusal of treatment and in 1 because of the development of peripheral neuritis.

TOXIC EFFECTS

The most alarming side effects were those involving the nervous system. The gastrointestinal tract, the cardiovascular system, the skin and formed elements of the blood also exhibited evidence of deleterious effects of phenytoin sodium. Each patient presented more than one symptom of a disquieting side effect involving various organs.

Ataxia, tremor and nystagmus were the most frequent symptoms reflecting toxic action on the nervous system. The ataxia was of the cerebellar type and the Babinski-Weil sign was frequently elicited. Many of the patients were irritable and apprehensive and said they were "jittery." The most serious complication was the development of an encephalopathy or a psychosis necessitating institutionalization. An encephalopathy occurred in 4 cases. A loss of weight in our experience was an indication of the development of toxic symptoms leading to an encephalopathy. One patient aged 15 who had a remission for six months while on phenytoin sodium therapy began losing weight gradually for a period of four months, although she said that she was eating too much. Her attention was wavering for several weeks and then she became somnolent. She had no subjective complaints but she walked slowly and stared as though in a trance. Then she complained of dizziness and mild nausea. She became very sleepy, mumbled to herself and was very unsteady in gait. Nystagmus was present laterally and vertically. A positive Babinski-Weil reaction was elicited. There was considerable swaying during the Romberg test. There was a facial weakness on the right side, hyperactive deep reflexes, absent superficial abdominal reflexes and no pathologic reflexes. She answered to questions only with yes or no very slowly. She became semistuporous.

This type of encephalopathy had developed in 4 cases. The psychotic behavior that occurred in 6 cases was characterized by a confusional paranoid state with significant irritability.

There were 2 children who had tantrums of temper consisting of stamping on the floor, walking around in circles and throwing themselves on the floor while on treatment. This behavior had not occurred on previous medication and their behavior may have been due to the toxic effects of phenytoin sodium. Other side effects involving the nervous system were vertigo and dizziness, paresthesias, peripheral neuritis (1 patient), headache, visual disturbances including blurring of vision and diplopia, insomnia, somnolence and general weakness.

Two of the patients developed status epilepticus, 1 after four weeks on phenytoin sodium 0.4 Gm. daily and the other after a week of treatment with 0.3 Gm. daily and phenobarbital 2¼ grains (0.15 Gm.) daily. Five patients had an increase in the frequency of spells. Others have reported, as already mentioned, status epilepticus as a complication of phenytoin sodium. It is possible that one of the toxic effects of phenytoin sodium is an increase in the frequency of seizures and status epilepticus.

The heart was studied also by electrocardiography because some of the patients complained of precordial distress. Twenty-seven patients were studied by serial electrocardiograms. All but 2 showed definite changes on a maximal dose of phenytoin sodium for each patient. Thirteen, or approximately 50 per cent, showed prolongation of the PR interval of from two hundredths to four hundredths second. Twenty-one, or 78 per cent, showed a decrease in the amplitude of the T wave. In 3 cases there were P wave changes and in 1 case there was a significant alteration of the QRS complex. In all cases, after the drug was discontinued, the electrocardiographic pattern returned toward the normal for each patient. For example, in 1 patient an electrocardiogram taken six weeks after the beginning of treatment showed evidence of a heart block. This patient complained of precordial oppression. Successive electrocardiograms showed an increase in the PR interval and he continued to complain of precordial distress.

Toxic Effects of Phenytoin Sodium Analyzed According to the Various Organs Involved

	Number of Patients
Nervous system	
Psychosis	6
Ataxia	17
Nystagmus	18
Vertigo and dizziness	4
Apprehensiveness and irritability	21
Paresthesias	5
Peripheral neuritis	1
Headache	2
Visual disturbances	10
Insomnia	5
Somnolence	1
Weakness	6
Tremor	15
Status epilepticus	2
Encephalopathy	4
Behavior disturbances	2
Cardiovascular system	
Electrocardiographic changes	32
Subjective complaints (precordial distress)	5
Edema of legs	1
Gastrointestinal system	
Nausea and vomiting	13
Anorexia	3
Abdominal pain	2
Weight loss	11
Gingival hyperplasia	17
Skin	
Scarlatiniform rash with fever	1
Rash and pruritus	6
Urine	
Albuminuria	6
Blood	
Secondary anemia	3
Eosinophils	9
Basophils	4
Increase in phosphatase	10

Phenytoin sodium was discontinued and the electrocardiograph was normal after a few months. Seven more patients not studied serially showed on the electrocardiograph a prolongation of the PR interval. One patient had edema of the legs.

The report by Williamson [12] of cardiac involvement as a result of treatment with phenytoin sodium is relevant in connection with the electrocardiographic changes that we have found. Three of his patients who had no history of cardiac or renal disease did have changes in the cardiac rate during the time that other toxic signs were present. One patient aged 20 had a simple bradycardia of 52 beats a minute three months after beginning treatment. Another, aged 58, had a bradycardia of 44 beats a minute with very frequent ventricular extrasystoles five weeks after starting treatment with phenytoin sodium. The patient complained of weakness, breathlessness and swelling of the ankles and showed cardiac dilatation, inversion of the T wave and clinical signs of cardiac insufficiency. The third patient had paroxysmal tachycardia which may merely have been coincidental and not due to treatment.

The other side effects due to phenytoin sodium as given in the table have at one time or another been reported by others, as mentioned in the survey of the literature. Although nausea and vomiting was quite frequent and may have been due to gastric irritability caused by the drug, the toxic effects as observed in 1 case simulating an acute abdominal condition is a more serious complication. The patient was a girl aged 19 who was given phenytoin sodium overlapping and substituting phenobarbital. When the dose of phenytoin sodium reached 0.6 Gm. a day a generalized weakness, severe abdominal pain, nausea and vomiting developed. There was no fever and the leukocyte count was normal. Phenytoin sodium was discontinued for a week and the symptoms disappeared. When treatment with phenytoin sodium was resumed the patient experienced the same symptoms within a week. She again recovered when phenytoin sodium was discontinued. When treatment with phenytoin sodium was begun a third time and she again had severe gastrointestinal symptoms she refused to take any more of the drug.

The loss of weight mentioned by others was also observed in some of our cases. The weight loss ranged from 1 to 22 pounds (450 Gm. to 9.1 Kg.). Fourteen patients lost weight, 11 gained and the others maintained the weight they had before treatment. Seventeen patients had a gingival hyperplasia, a condition first reported by Kimball.[5]

The only significant change noted in blood chemistry studies was an increase in the serum phosphatase. The phosphatase value after various periods of treatment ranged from 7.92 to 18.59 mg. per hundred cubic centimeters. The average value was 10.77. This is of interest in relation to hepatic involvement, since Mandelbaum and Kane [16] reported a case in which there was enlargement of the liver and spleen with an increase in serum phosphatase.

Seven patients are still on treatment with phenytoin sodium. These patients were continued on treatment because phenytoin sodium definitely exerted favorable influences on their seizures. These patients also had side effects from phenytoin sodium but not sufficiently serious to indicate cessation of phenytoin sodium since the side effects were offset by the remissions caused by phenytoin sodium. These patients had the complications mentioned in the table, but at the present time, more than two years after treatment, they are for the most part free of them.

Of the 7 patients still on treatment with phenytoin sodium, 6 have had remissions from seizures of from ten to seventeen months and 1 is free from seizures for periods of about two months. Previously these patients had not responded favorably to bromides, to phenobarbital or to both.

SUMMARY

Forty-one patients with epilepsy were treated with phenytoin sodium according to the method of Merritt and Putnam. All the patients showed some side effect of the drug, ranging from apprehensiveness and irritability, present in 21 patients, to the development of an encephalopathy, in 4 patients. Side effects involved chiefly the nervous system and ataxia, vertigo, blurring of vision, nystagmus, tremors, insomnia and somnolence occurred. Status epilepticus, a paranoid confusional psychosis and encephalopathy were observed.

Of particular interest in relation to the cardiovascular system was electrocardiographic evidence of involvement of the heart. There were also toxic effects on the gastrointestinal system and the skin.

303 East Chicago Avenue.

Clinical Notes, Suggestions and New Instruments

FAMILIAL HEREDITARY EDEMA

MILROY'S DISEASE

ROBERT L. STERN, M.D., CAMP CALLAN, CALIF.
1st Lieut., M. C., U. S. Army

The occurrence of familial hereditary edema, also known as Milroy's disease, hereditary trophedema and hereditary or congenital elephantiasis, is rare, particularly when a continued familial incidence can be demonstrated. Search of the literature reveals that fewer than fifty families with this hereditary syndrome have been reported. The following case is presented because such reports are rare and because of the studies, manifestations and improvement on treatment.

REPORT OF CASE

A. W. S., a white man, aged 25, unmarried, a selectee in the United States Army, was admitted to the Station Hospital, Camp Callan, California, Aug. 4, 1941 because of pain, swelling and mottled redness of the right foot. In civilian life he had been a painter. His home was in the Middle West. Since his induction in the army seven weeks prior to entering the hospital, he had been engaged in the usual training and drilling on the camp grounds. He stated that there had been some degree of pitting and swelling of the right foot as long as he could remember. His mother had told him that this had started when he was about a year old, or about the time he might have been expected to start walking. The condition has always been confined to the right foot. It has given him varying degrees of distress from none at all to the condition present on hospitalization. Symptoms have always been more severe during the summer months. Activity has little effect except that when he is on his feet a great deal the swelling is a little more noticeable. This clears somewhat when he is at rest with the foot elevated, but he is never without some slight degree of swelling. The foot has never been frostbitten or injured, nor has the skin ever blistered. He has never had an infection of the leg or abdomen. The patient has been a heavy smoker all his adult life, but there is no correlation between the amount of his smoking and the swelling of the foot.

The patient has had numerous and varied treatments in civilian life without relief of the condition. When the swelling is at its maximum or when acute episodes of redness and pain occur he experiences a sensation of shooting pain going up and down the bone between the ankle and the knee.

The patient was cooperative and intelligent. He stated that he had never had any serious illness and that he had had no venereal disease of any type. His only operation was a herniorrhaphy on the left side in 1930. His height was 65½ inches (168 cm.) and his weight 138 pounds (62.6 Kg.); his temperature peak was 100.6 F., pulse peak 100 on the day of entry and blood pressure 130 systolic and 85 diastolic. Physical examination was essentially negative except for premature baldness of the crown of the head, a well healed, freely movable inguinal scar on the left side and hot, red swelling of the right foot over the dorsum and sides from the ankle to but not including the toes, although the toes were slightly swollen. There were small petechial hemorrhages on the lateral aspect of the foot but nowhere else. The foot was moderately tender to deep pressure, and active motion was fair. There was no lymphangitis and no adenopathy.

Roentgen examination of the foot was reported by Lieutenant Sachs, roentgenologist, as follows: "The bones of the right ankle joint are within normal limits. Soft tissue studies of the ankle reveal a soft tissue swelling. There is no evidence of calcification of the soft tissue" (fig. 2).

Urinalysis was essentially negative; the blood Kahn reaction was negative. A blood count revealed the hemoglobin level

From the Coast Artillery Replacement Center, Station Hospital.

80 per cent, erythroctyes 3,850,000, leukocytes 9,050 with 76 per cent polymorphonuclear neutrophils. The blood sedimentation rate was 46 mm. (normal 5 to 10 mm.) and the blood uric acid content 3.5 mg. per hundred cubic centimeters.

Treatment consisting of administration of sulfathiazole and elevation of the foot was instituted and continued for one week. On the fourth day the temperature, which had remained at 99 to 100 F., returned to normal and continued at that level thereafter. At that time the redness of the foot had cleared and the pain had greatly diminished. On the fifth day of hospitalization the blood sedimentation rate was 30 mm., with the blood count approximately as before. The swelling of the foot persisted unchanged, however, and he was transferred to a medical ward. At the end of his second week in the hospital the cellulitis and the cutaneous irritation were completely cleared, but the swelling of the foot and ankle remained about the same. Examination of scrapings of the skin of the foot and between the toes failed to reveal any evidence of mycotic infection. Repeated urinalyses remained essentially negative. Blood counts were normal except for the persistent, moderately low erythrocyte and hemoglobin determinations. He continued to have occasional aching pain in the leg, but this was intermittent and slight, and he was ambulatory. Bed rest with elevation made little impression on the swelling, which was now firm but not brawny, pitted on pressure, was not tender and extended to a point about half way to the knee. The skin was now smooth, warm, of normal color and somewhat thickened. Both dorsalis pedis arteries pulsated normally.

On August 23, the twentieth hospital day, because of the persistent swelling and the important revelation of the foot swelling since infancy, familial hereditary edema was suspected and the patient questioned closely about hereditary factors. In regard to these, he was positive about the following: His maternal grandfather had the same type of swelling, confined to the left foot, with onset known to have occurred at the age of 16 years; his maternal great grandfather was said to have had the same condition, and the patient's mother has had unexplained swelling of both her legs since the age of 28. His grandfather had thirteen siblings, none of whom had a similar condition; his mother had three sisters, all of whom died in infancy, and two brothers who have no evidence of a similar condition. The patient had one brother and one sister who did not have a similar condition. The manifestations and history were deemed sufficient to establish a diagnosis of familial hereditary edema especially after further studies to exclude other conditions were made.

The sedimentation rate was now a normal 11 mm., the stool was found clear of pathogenic parasites and the total serum

Fig. 1.—Patient's legs just previous to mercupurin therapy, showing the swelling of the right foot.

protein was 6.9 mg. per hundred cubic centimeters. Roentgenograms of the chest, the pelvis and hip joints revealed a normal appearance. The blood pressure in the legs with the systolic determined by palpation of the first pulsation in the dorsalis pedis arteries was 168 in the left leg and 138 in the right leg. The venous pressure in the right leg was 10.5 cm., and at the same midcalf level in the left it was 9 cm. The circulation time from the midcalf of the left leg to the tongue, with the use of decholin, was ten seconds and of the right leg twenty seconds. The left leg-tongue time was determined first and, although a time lapse was allowed with the patient

Fig. 2.—Front and side view of the patient's right ankle and foot.

continuing at absolute rest, the difference in the circulation times was probably partially due to a dulled taste perception for the agent used.

On September 16, thirty-nine days after the redness and evidence of cellulitis had cleared, the comparative circumferences of the legs were, at the malleoli: right leg 12¼ inches (31.5 cm.), left 10 inches (25 cm.) at a level 3 inches (7.6 cm.) about the malleoli: right 9½ inches (24.5 cm.), left 8½ inches (22 cm.), the left leg having been, of course, of normal appearance throughout the period of observation. Above these levels the two legs were of the same circumference (fig. 1).

On September 17, the forty-fourth hospital day, because the swelling remained the same despite long periods of bed rest and because the patient still had intermittent aching of the leg, 2 cc. of mercupurin was administered intravenously. During twenty-four hours the patient had a fairly good diuresis, which it was impossible to measure accurately because the patient had to be out of the hospital part of the day, and his weight dropped from 136 to 133 pounds (61.7 to 60. 3 Kg.). The right ankle and foot were definitely less swollen, the measurements now having decreased to 11 inches (28 cm.) in circumference at the malleoli and 8¾ inches (23 cm.) at a level 3 inches above the malleoli. With the reduction of the swelling of the foot, the intermittent distress in the foot cleared entirely.

Within the week he was discharged from the hospital in continued excellent general condition and was discharged from the army to his home by a Certificate of Disability Discharge. He was advised either to have mercupurin therapy whenever the leg caused distress or to try other suggested long term therapy under the supervision of a private physician. He reported by mail on October 13 that he continues to be in good general health and has no distress whatever in the leg, although some swelling persists.

SUMMARY AND CONCLUSIONS

1. A case of familial hereditary edema with a maternal family incidence in four generations has been reported because of the rarity of the condition described and because of the studies and observations made.

2. The case is further unusual because it is generally regarded that this type, the congenital as differentiated from the acquired,

which occurs later in life, does not present the acute pain and inflammatory episodes which this patient suffers.

3. The use of mercupurin to relieve the swelling gave complete relief from intermittent aching pain, which thereby is apparently demonstrated to be due to the swelling and not intrinsic with the syndrome.

PSITTACOSIS

HENRY ALICANDRI, M.D., BROOKLYN

Psittacosis, a highly communicable disease, has been transmitted to man by parrots, parakeets, love birds and rarer birds of the parrot family.

This communication is of interest because it presents an isolated case of psittacosis in which the only exposure to a bird was to the common pigeon; this possible source of infection warrants closer investigation.

REPORT OF CASE

L. M., a white man aged 35, born in the United States, a policeman, collapsed suddenly while on duty on Oct. 8, 1941. I saw him a few hours later, at which time he complained of fatigue, pain in the left lower portion of the chest extending from the axilla to the precordium, slight cough and blood tinged sputum. He also stated that he had had chills and fever and a "grippy" feeling for two or three days.

The past history showed no previous illness or operation. He was given sulfathiazole, and for the next six days the temperature varied from 100 to 103 F. The pulse rate was 70 to 80 and the heart sounds were distant and of poor quality.

On October 15 the pain in the chest became severe and the temperature rose to 104.5 F. The patient was flushed and the membranes were cyanotic; he was admitted to the Bay Ridge Hospital.

A roentgenogram made on admission revealed that the lung roots were clouded by central pneumonitis, and there was an exudative spread of this process into the lower lobe of the right lung. The heart appeared grossly enlarged to the left. The impression was that of influenzal pneumonia and mitral valvular disease. The heart sounds were weak at the apex, and the P wave in lead 2 was accentuated.

Examination of the blood on October 16 showed hemoglobin 96 per cent, erythrocytes 4,850,000, leukocytes 16,400, polymorphonuclear leukocytes 76 per cent, small lymphocytes 20 per cent, large mononuclear cells 3 per cent and eosinophils 1 per cent. On October 18 the blood showed hemoglobin 97 per cent, erythrocytes 4,950,000, leukocytes 17,650, polymorphonuclear leukocytes 70 per cent, small lymphocytes 22 per cent, large mononuclear cells 5 per cent and basophils 1 per cent. On October 20 the blood showed hemoglobin 84 per cent, erythrocytes 4,350,000, leukocytes 26,900, polymorphonuclear leukocytes 91 per cent, small lymphocytes 8 per cent and large mononuclear cells 1 per cent. The blood count on October 24 was hemoglobin 80 per cent, erythrocytes 4,480,000, leukocytes 9,800, polymorphonuclear leukocytes 78 per cent, small lymphocytes 11 per cent and large mononuclear cells 8 per cent. On October 27 the leukocytes numbered 12,500, polymorphonuclear leukocytes 6 per cent, small lymphocytes 24 per cent, large mononuclear cells 6 per cent and eosinophils 3 per cent.

Blood cultures showed no growth. Analysis of the urine revealed occasional casts and white blood cells but no albumin or sugar. The diazo test gave negative results. Pneumococci (of types I to XXXIII) were not found in the sputum. Mouse injection did not yield pneumococci or tubercle bacilli. The Wassermann reaction was negative. Agglutination tests for typhoid, paratyphoid and A and B brucellosis and typhus all gave negative results.

The temperature was spiky the first week, ranging from 100.5 to 104.5 F., and the pulse rate was comparatively slow, 80 to 120. The second week the curve was typhoidal, and the last two weeks the temperature curve was flat, at 99.5 F. Respirations were for the most part normal.

Another roentgen examination, on November 7, showed left ventricular hypertrophy. There was unresolved, diffuse, patchy pneumonitis.

Treatment was given with drugs of the sulfonamide series, circulatory supportive drugs and the use of an oxygen tent for three weeks.

In view of the clinical aspect of the patient, the roentgen data and the failure of response to treatment with sulfonamide derivatives, a tentative diagnosis of psittacosis was considered for investigation. A specimen of the patient's serum was sent to Dr. Karl Meyer of the George Williams Hooper Foundation in San Francisco, who reported on October 30 a strongly positive reaction (4 plus) for psittacosis (the antigen fixed in a dilution of 1:256).

Except for the occurrence of phlebitis of the right leg, recovery after the third week was uneventful, and the patient was discharged from the hospital on November 15. Subsequent roentgen and electrocardiographic examination was reported as giving normal results.

The only contact with birds known was with pigeons, some of which the New York City Department of Health obtained and forwarded to Dr. Karl Meyer in San Francisco.

1001 Sixty-Fourth Street.

SPONTANEOUS ELIMINATION OF A LIPOMA FROM THE SIGMOID FLEXURE

SYLVAN D. MANHEIM, M.D., AND HENRY PESKIN, M.D., NEW YORK

Benign tumors of the gastrointestinal tract are not frequent, and lipomas constitute but a small portion of those which do occur. Staemmler,[1] in a series of 17,000 consecutive postmortem examinations, found only 9 lipomas, an incidence of 0.05 per cent. In a series of 3,924 consecutive autopsies at the Mayo Clinic, Comfort[2] found 20 intestinal lipomas, an incidence of 0.5 per cent. The discrepancy in these two series may have been due to the difference in size of the series or to the degree of care in searching for lipomas.

From time to time there have been reports in the literature of spontaneous elimination of gastrointestinal lipomas. In the sixty-five years from 1870 to 1935, 15 cases have been reported, 1 reported by Ninaus[3] might not be properly included because an invagination of the intestine occurred and the tumor was expelled, together with the involved portion of intestine. In 1939 Odstrcil[4] reported 3 more instances of spontaneously expelled lipomas, all of which occurred within a period of three years. In 1940 Backenstoe[5] reported a case of submucous lipoma of the cecum spontaneously eliminated. To these 18 cases we wish to add the report of a case which was seen in the rectal clinic of the Mount Sinai Hospital. Before presenting this, however, several aspects of this phenomenon are worthy of note. Various theories have been offered in explanation of the mechanism of expulsion. One theory offered is that invagination of the affected area of the intestine results in necrosis with sequestration of the intussuscepted portion. Another is that the mucous membrane overlying the lipoma is torn at its base and the tumor slips through the mucosal defect. In our case, only a small portion of one end of the tumor was covered with mucous membrane, suggesting a possible thinning out and tearing of this membrane due either to direct trauma or to loss of blood supply as a result of pressure necrosis.

The symptoms have been varied. In some instances bleeding, usually intermittent, has been the chief or only symptom. In

From the Rectal Clinic and Surgical Service of Dr. John H. Garlock.

1. Cited by Odstrcil.[4]

2. Comfort, M. W.: Submucous Lipoma of the Gastrointestinal Tract with a Report of Twenty-Eight Cases, Surg., Gynec. & Obst. **52**: 108-118 (Jan.) 1931.

3. Ninaus, cited by Stetten, D.: The Submucous Lipoma of the Gastrointestinal Tract, Two Successfully Operated Cases and Analysis of the Literature, Surg., Gynec. & Obst. **9**: 156-176 (Aug.) 1909.

4. Odstrcil, B.: Ueber spontane Elimination von Darmlipomen, Virchows Arch. f. path. Anat. **305**: 413-431, 1939.

5. Backenstoe, G. S.: Spontaneous Expulsion of Submucous Lipoma of Cecum, Pennsylvania M. J. **44**: 21 (Oct.) 1940.

others pain has been the patient's chief complaint. In several of the cases reported intestinal obstruction or intussusception caused the patient to seek medical assistance. In our case, mucopurulent discharge and intermittent diarrhea led to the tentative diagnosis of colitis by her family physician. There are also cases in which a roentgen examination suggested the presence of a neoplasm for which a laparotomy was performed.

REPORT OF CASE

A white woman aged 47 was referred to the Rectal Clinic of the Mount Sinai Hospital by her family physician. She gave a history of intermittent diarrhea accompanied by blood and a mucopurulent discharge of many years' duration. In addition, she stated that she had been totally unable to have a bowel movement for the week prior to her initial visit. On rectal examination, after cleansing enemas had been given, the anus and rectum were found to be essentially normal. The sigmoidoscope was passed full length (25 cm.) and blood was seen to be coming down from above this point. A roentgen examination of the colon with a barium enema was done, which was reported to show a filling defect of the midsigmoid region about 6 cm. in length, suggesting a polypoid type of neoplasm with intussusception in this area. The remainder of the colon was normal (fig. 1).

Fig. 1.—Filling defect of midsigmoid.

On the basis of these observations the patient was advised to enter the hospital for operation. She refused and instead returned to the clinic two weeks later to report that she had had severe abdominal cramps forty-eight hours previously. Accompanying these cramps she experienced an urge to defecate and, when her bowels moved, passed a large amount of blood and a tumor, which she retrieved and brought with her (fig. 2).

The pathologic report on the tumor was that it was a lipoma partially covered by necrotic sigmoidal mucosa showing acute inflammation. The specimen was an oval mass received in fixative and measured 6 by 4 by 4 cm. Three quarters of the mass was fairly soft; the remainder of the surface had a dirty greenish brown color and was somewhat more firm and granular.

Roentgen examination taken three weeks after the spontaneous elimination of the tumor revealed "a filling defect in the midsigmoid region about 3 cm. in length" (fig. 3). Although the appearance was much less pronounced than at the previous examination, there was still evidence to suggest a small polypoid mass with intussusception. Another examination four weeks later presented the same picture. The patient has been seen at intervals over a period of five months; during this time she has been entirely symptom free.

The persistent roentgen signs suggest the possibility of another submucous lipoma being present, and because of that the patient will be kept under observation.

In reviewing the cases reported in the literature, we find that they were almost equally divided as to sex. The youngest patient was 16 years of age, the oldest was 87. The majority seemed to have been in the fifth or sixth decade. The exact location of these tumors was not always accurately determined, but the majority seemed to have originated in the colon. Some

Fig. 2.—Lipoma partially covered by necrotic sigmoid mucosa.

of these tumors were merely 2 cm. in diameter, while that reported by Afezou [1] was supposed to have been the size of a child's head. It should be noted here that the lipoma in the latter instance originated in the rectal ampulla, which may account for the large size that it attained without producing serious obstructive symptoms. Some of these lipomas were polypoid, others were sessile and in 2 instances the patient suffered from multiple lipomas, which were expelled over a period of weeks.

Fig. 3.—Appearance of sigmoid three weeks after elimination of lipoma.

SUMMARY

A lipoma of the midsigmoid was spontaneously expelled with complete relief of symptoms. Lipomas constitute only a small percentage of the benign tumors of the intestinal tract, which in themselves are infrequent. Surgical intervention resulting from early diagnosis may account for the fact that only 20 instances of spontaneous expulsion of lipomas have been reported in the last seventy years.

336 Central Park West—41 West Ninety-Sixth Street.

Council on Pharmacy and Chemistry

REPORTS OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

AUSTIN E. SMITH, M.D., Acting Secretary.

PROGESTERONE

The Committee on Revision of the U. S. P. XII has signified the intention of including progesterone, the corpus luteum hormone, in U. S. P. XII. The Council on Pharmacy and Chemistry has already published its preliminary report (J. A. M. A. **116**:1523 [April 5] 1941) on progesterone, in which it was stated that the inclusion of this substance in N. N. R. was not warranted because of the lack of adequate evidence that progesterone therapy was conclusively established in any of the clinical indications for which it has been recommended. In its report the Council stated that further consideration of progesterone for acceptance would be deferred until additional scientific evidence becomes available, establishing definitely its usefulness.

In view of the discrepancy between the Council's view and that of the Committee on Revision of the U. S. P., the therapeutic indications for progesterone were again reviewed in the light of the latest available evidence. The Council, however, was unable to alter its opinion as to the status of progesterone therapy, although the potentialities of this substance were recognized. The Council, therefore, reaffirms its previous published opinion regarding the status of progesterone.

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

AUSTIN E. SMITH, M.D., Acting Secretary.

CALCIUM GLUCONATE (See New and Nonofficial Remedies, 1941, p. 176).

The following dosage forms have been accepted:

Wafers Calcium Gluconate (Flavored)-Upjohn, 0.96 Gm. (15 grains): Each wafer contains calcium gluconate, U. S. P., 15 grains with sugar, talc, dye and oil of wintergreen for flavoring.

Prepared by The Upjohn Company, Kalamazoo, Mich.

Ampoules Calcium Gluconate Solution 10% W/V Stabilized with Calcium d-Saccharate 1% W/V-Upjohn, 10 cc.: Each ampul contains a sterile distilled water solution of calcium gluconate, U. S. P., 1.0 Gm., stabilized with calcium *d*-saccharate 0.1 Gm.

Prepared by The Upjohn Company, Kalamazoo, Mich.

CALCIUM *d*-SACCHARATE: The calcium *d*-saccharate used as a stabilizing agent in these solutions of calcium gluconate so stabilized complies with the following tests and standards:

Calcium *d*-saccharate occurs as a fine, white, odorless tasteless powder, which is stable in air. It is slightly soluble in water, ether, alcohol and chloroform. A saturated solution of calcium *d*-saccharate is neutral to litmus and possesses a *p*H of about 6.0.

Transfer about 0.1 Gm. of calcium *d*-saccharate to a test tube, add 10 cc. of water and 1 cc. of diluted hydrochloric acid: the resultant solution is clear and colorless. To this solution add 5 cc. of ammonium oxalate solution: a white precipitate appears, which is soluble in diluted hydrochloric acid.

Dissolve 0.5 Gm. of calcium *d*-saccharate in 10 cc. of water and 2 cc. of diluted hydrochloric acid, and boil the solution for two minutes. Cool, add 5 cc. of sodium carbonate solution, allow to stand for five minutes, dilute to 20 cc. with distilled water and filter. Add 5 cc. of the filtrate to 2 cc. of alkaline cupric tartrate solution and boil for one minute: no red precipitate is formed *(dextrose and sucrose)*.

One Gm. of calcium *d*-saccharate shows no more chloride when tested with diluted nitric acid and silver nitrate solution than 1 cc. of fiftieth-normal hydrochloric acid. A 2 Gm. portion of calcium *d*-saccharate shows no more sulfate than corresponds to 1 cc. of fiftieth-normal sulfuric acid when tested with diluted hydrochloric acid and barium chloride solution. Dissolve 1 Gm. of calcium *d*-saccharate in 10 cc. of distilled water and 3 cc. of diluted hydrochloric acid; add 10 cc. of hydrogen sulfide solution: no precipitate appears, and the color is not darker than a faint brown *(heavy metals)*.

Transfer approximately 0.4 Gm. of calcium *d*-saccharate, dried over sulfuric acid and accurately weighed, to a 250 cc. beaker, and dissolve in 100 cc. of distilled water and 2 cc. of hydrochloric acid. Add an excess of ammonium oxalate solution, heat to boiling, and slowly neutralize with ammonia water, with stirring. Digest the mixture on a water bath for one hour, filter on hardened filter paper and wash thoroughly with warm distilled water. Puncture the filter paper, wash the precipitate into a beaker by means of a stream of hot distilled water, followed by 30 cc. of diluted (1:3) sulfuric acid. Heat the solution to 60 C. and titrate with tenth-normal potassium permanganate: the calcium oxide content is not less than 17.3 and not more than 17.7 per cent.

SODIUM *r*-LACTATE ONE-SIXTH MOLAR (See Revised Supplement to New and Nonofficial Remedies, 1941, p. 27).

The following brand has been accepted:

THE UPJOHN COMPANY, KALAMAZOO, MICH.

Sodium Lactate (Racemic) ⅙ Molar (1.87% W/V: 500 cc. and 1,000 cc. Upjohn Infusion Bottles. Each hundred cubic centimeters contains 1.87 Gm. of sodium *r*-lactate in sterile distilled water.

BLENDED OIL CONTAINING VITAMINS A AND D.—A mixture of fish and/or vegetable oils to which viosterol may be added. The vitamin A content is not less than 1,800 U. S. P. units per gram and the vitamin D content not less than 175 U. S. P. units per gram.

Actions and Uses.—See article Vitamins A and D Preparations, N. N. R., 1941, page 562.

Dosage.—See article Vitamins A and D Preparations, N. N. R., 1941, page 562.

Blended oil containing vitamins A and D occurs as a thin, liquid oil having a fishy but not rancid odor and a fishy taste. It is insoluble in water, slightly soluble in alcohol and soluble in chloroform, ether, benzene, ethyl acetate and carbon disulfide. The specific gravity is from 0.918 to 0.929 at 25 C. The refractive index is from 1.474 to 1.479 at 25 C.

A solution of one drop of blended oil containing vitamins A and D in 1 cc. of chloroform, when shaken with one drop of sulfuric acid, acquires a blue color, gradually changing to purple. Fill a tall cylindric tube of about 120 cc. capacity with the oil and maintain at 0 C. for five hours: the oil remains clear and fluid and deposits no solid material.

Dissolve 2 Gm., accurately weighed, of blended oil containing vitamins A and D in 30 cc. of a mixture of equal parts of ether and alcohol, previously neutralized to phenolphthalein, and boil gently under a reflux condenser for ten minutes. Cool and titrate the mixture with tenth-normal sodium hydroxide to the production of a pink color which persists for thirty seconds; not more than 1 cc. of tenth-normal sodium hydroxide is required *(free acid)*. The unsaponifiable matter in blended oil containing vitamins A and D is not more than 1.5 per cent when determined according to the method as given in the U. S. P. XI. The iodine value is not less than 145 nor more than 180. The saponification value is not less than 186 nor more than 202.

MEAD JOHNSON & CO., INC., EVANSVILLE, IND.

Mead's Blended Oil Containing Vitamins A and D: bottles 4 fluid ounces.

U. S. patent 1,680,818 (Aug. 14, 1928; expires 1945) and 1,861,136 (Aug. 9, 1934; expires 1951) under license of the Wisconsin Alumni Research Foundation.

Irradiated ergosterol, prepared by the method described under Mead's Viosterol in oil, is added to fish liver oil, sardine oil and maize oil, and the finished product is required to have a vitamin A potency of not less than 1,800 units (U. S. P.) per gram and not less than 175 units (U. S. P.) of vitamin D per gram.

DEXTROSE (See New and Nonofficial Remedies, 1941, p. 179).

The following additional dosage forms have been accepted:

HOSPITAL LIQUIDS, INC., CHICAGO.

Dextrose 20% (W/V) in Distilled Water in Filtrair Container: 500 cc., 1,000 cc. and 2,000 cc. bottles. Each hundred cubic centimeters contains dextrose-U. S. P. 20 Gm.

Dextrose 50% (W/V) in Distilled Water: 50 cc. and 100 cc. vials. Each hundred cubic centimeters contains dextrose-U. S. P. 50 Gm.

Dextrose 2½% (W/V) in Physiologic Sodium Chloride Solution in Filtrair Container: 500 cc., 1,000 cc. and 2,000 cc. bottles. Each hundred cubic centimeters contains dextrose-U. S. P. 2.5 Gm. and sodium chloride-U. S. P. 0.9 Gm.

Dextrose 7½% (W/V) in Physiologic Sodium Chloride Solution in Filtrair Container: 500 cc., 1,000 cc. and 2,000 cc. bottles. Each hundred cubic centimeters contains dextrose-U. S. P. 7.5 Gm. and sodium chloride-U. S. P. 0.9 Gm.

Dextrose 20% (W/V) in Physiologic Sodium Chloride Solution in Filtrair Container: 500 cc., 1,000 cc. and 2,000 cc. bottles. Each hundred cubic centimeters contains dextrose-U. S. P. 20 Gm. and sodium chloride-U. S. P. 0.9 Gm.

Dextrose 5% (W/V) in Isotonic Solution of Three Chlorides in Filtrair Containers: 500 cc., 1,000 cc. and 2,000 cc. bottles. Each hundred cubic centimeters contains dextrose-U. S. P. 5 Gm., sodium chloride-U. S. P. 0.7 Gm., potassium chloride-N. F. 0.03 Gm. and calcium chloride-U S. P. 0.025 Gm.

Dextrose 10% (W/V) in Isotonic Solution of Three Chlorides in Filtrair Container: 500 cc., 1,000 cc. and 2,000 cc. bottles. Each hundred cubic centimeters contains dextrose-U. S. P. 10 Gm., sodium chloride-U. S. P. 0.7 Gm., potassium chloride-N. F. 0.03 Gm. and calcium chloride-U S. P. 0.025 Gm.

SILVER NITRATE (See New and Nonofficial Remedies, 1941, p. 499).

The following dosage form has been accepted:

THE WM. S. MERRELL CO., CINCINNATI.

Solution **Silver Nitrate 1% W/V:** 0.5 cc. wax ampules.

ANTIPNEUMOCOCCIC SERUM, TYPE 1 (FROM RABBITS) (See New and Nonofficial Remedies, 1941, p. 447).

The following brand has been accepted:

LEDERLE LABORATORIES, INC., PEARL RIVER, N. Y.

Antipneumococcic Serum (Rabbit), Type 1: Vials, 20,000 and 50,000 units. A refined and concentrated globulin solution of pneumococcus antibodies prepared by immunizing rabbits against virulent cultures of the type 1 pneumococcus. It contains 0.4 per cent phenol and 1-50,000 phenyl mercuric acetate as a preservative.

ANTIPNEUMOCOCCIC SERUM, TYPE 2 (FROM RABBITS) (See New and Nonofficial Remedies, 1941, p. 448).

The following brand has been accepted:

LEDERLE LABORATORIES, INC., PEARL RIVER, N. Y.

Antipneumococcic Serum (Rabbit), Type 2: Vials, 20,000 and 50,000 units. A refined and concentrated globulin solution of pneumococcus antibodies prepared by immunizing rabbits against virulent cultures of the type 2 pneumococcus. It contains 0.4 per cent phenol and 1-50,000 phenyl mercuric acetate as a preservative.

ANTIPNEUMOCOCCIC SERUM, TYPE 3 (FROM RABBITS) (See New and Nonofficial Remedies, 1941, page 449).

The following brand has been accepted:

LEDERLE LABORATORIES, INC., PEARL RIVER, N. Y.

Antipneumococcic Serum (Rabbit), Type 3: Vials, 20,000 and 50,000 units. Also available in vials containing 100,000 units. Each package contains a vial of normal rabbit serum (1:10 dilution) for the conjunctival test. A refined and concentrated globulin solution of pneumococcus antibodies prepared by immunizing rabbits against virulent cultures of the type 3 pneumococcus. It contains 0.4 per cent phenol and 1-50,000 phenyl mercuric acetate as a preservative.

ANTIPNEUMOCOCCIC SERUM, TYPE 4 (FROM RABBITS) (See Revised Supplement, 1941, page 30).

The following brand has been accepted:

LEDERLE LABORATORIES, INC., PEARL RIVER, N. Y.

Antipneumococcic Serum (Rabbit), Type 4: Vials, 20,000 and 50,000 units. A refined and concentrated globulin solution of pneumococcus antibodies prepared by immunizing rabbits against virulent cultures of the type 4 pneumococcus. It contains 0.4 per cent phenol and 1-50,000 phenyl mercuric acetate as a preservative.

ANTIPNEUMOCOCCIC SERUM, TYPE 5 (FROM RABBITS) (See New and Nonofficial Remedies, 1941, page 449).

The following brand has been accepted:

LEDERLE LABORATORIES, INC., PEARL RIVER, N. Y.

Antipneumococcic Serum (Rabbit), Type 5: Vials, 20,000 and 50,000 units. A refined and concentrated globulin solution of pneumococcus antibodies prepared by immunizing rabbits against virulent cultures of the type 5 pneumococcus. It contains 0.4 per cent phenol and 1-50,000 phenyl mercuric acetate as a preservative.

ANTIPNEUMOCOCCIC SERUM, TYPE 7 (FROM RABBITS) (See New and Nonofficial Remedies, 1941, page 450).

The following brand has been accepted:

LEDERLE LABORATORIES, INC., PEARL RIVER, N. Y.

Antipneumococcic Serum (Rabbit), Type 7: Vials, 20,000 and 50,000 units. A refined and concentrated globulin solution of pneumococcus antibodies prepared by immunizing rabbits against virulent cultures of the type 7 pneumococcus. It contains 0.4 per cent phenol and 1-50,000 phenyl mercuric acetate as a preservative.

ANTIPNEUMOCOCCIC SERUM, TYPE 8 (FROM RABBITS) (See New and Nonofficial Remedies, 1941, page 451).

The following brand has been accepted:

LEDERLE LABORATORIES, INC., PEARL RIVER, N. Y.

Antipneumococcic Serum (Rabbit), Type 8: Vials, 20,000 and 50,000 units. A refined and concentrated globulin solution of pneumococcus antibodies prepared by immunizing rabbits against virulent cultures of the type 8 pneumococcus. It contains 0.4 per cent phenol and 1-50,000 phenyl mercuric acetate as a preservative.

ANTIPNEUMOCOCCIC SERUM, TYPE 14 (FROM RABBITS) (See THE JOURNAL, Dec. 13, 1941, page 2073).

The following brand has been accepted:

LEDERLE LABORATORIES, INC., PEARL RIVER, N. Y.

Antipneumococcic Serum (Rabbit), Type 14: Vials, 20,000 and 50,000 units. A refined and concentrated globulin solution of pneumococcus antibodies prepared by immunizing rabbits against virulent cultures of the type 14 pneumococcus. It contains 0.4 per cent phenol and 1-50,000 phenyl mercuric acetate as a preservative.

SOLUBLE IODOPHTHALEIN (See New and Nonofficial Remedies, 1941, p. 233).

Ampuls Iodeikon, 3.5 Gm.-Lakeside: Each ampul contains 3.5 Gm. of iodeikon (soluble iodophthalein).

Prepared by Lakeside Laboratories, Inc., Milwaukee.

VIOFORM-CIBA (See New and Nonofficial Remedies, 1941, p. 297).

The following additional dosage form has been accepted:

Tablets Vioform-Ciba, 250 mg.

SULFAPYRIDINE (See New and Nonofficial Remedies, 1941, p. 511).

The following dosage form has been accepted:

ENDO PRODUCTS, INC., RICHMOND HILL, N. Y.

Tablets Sulfapyridine: 0.5 Gm. (7½ grains).

MAGNESIUM TRISILICATE (See New and Nonofficial Remedies, 1941, p. 343).

The following dosage form has been accepted:

LAKESIDE LABORATORIES, INC., MILWAUKEE.

Tablets Magnesium Trisilicate: 0.49 Gm. (7½ grains).

AMNIOTIN (See New and Nonofficial Remedies, 1941, p. 375).

The following additional dosage forms have been accepted:

Amniotin Capsules, 10,000 International Units.

Amniotin in Corn Oil, 20 cc. vials, 2,000 International Units per cc.

Amniotin in Corn Oil, 10 cc. vials, 10,000 International Units per cc.

ASCORBIC ACID-U. S. P. (See New and Nonofficial Remedies, 1941, p. 557).

The following dosage form has been accepted:

Tablets Ascorbic Acid-SMACO, 100 mg.

Prepared by the S. M. A. Corporation, Chicago.

SUSPENSION OF EPINEPHRINE IN OIL, 1:500 (See New and Nonofficial Remedies, 1941, p. 255).

Epinephrine in Oil, 1:500-Lakeside.—A brand of suspension of epinephrine in oil, 1:500-N. N. R.

Manufactured by The Lakeside Laboratories, Inc., Milwaukee. No U. S. patent or trademark.

Ampules Epinephrine in Oil, 1:500-Lakeside, 1 cc.: A suspension of 2 mg. powdered epinephrine crystals in 1 cc. of sesame oil.

DIGITALIS (See New and Nonofficial Remedies, 1941, p. 204).

ENDO PRODUCTS, INC., RICHMOND HILL, N. Y.

Tablets Digitalis: ¾ grain (½ U. S. P. unit) and 1½ grains (1 U. S. P. unit) (enteric coated). The tablets are first coated with a white shellac and then sugar-coated green.

AMINOPYRINE (See New and Nonofficial Remedies, 1941, p. 399).

The following dosage form has been accepted:

THE WM. S. MERRELL CO., CINCINNATI.

Tablets Aminopyrine: 0.324 Gm. (5 grains).

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, APRIL 4, 1942

THE ATLANTIC CITY SESSION

Several Fellows of the American Medical Association have suggested that the Atlantic City session might be removed to the interior of the country because of the possibility of increased danger on the sea coast. To obtain an official expression of opinion on this point, the editor of THE JOURNAL consulted Robert P. Patterson, Under Secretary of War, in Washington. Mr. Patterson writes:

Dear Dr. Fishbein:

I have your letter of March 23 raising the question as to whether it would be advisable to move the convention of the American Medical Association away from Atlantic City.

I know of no valid reason why this convention should not be held in Atlantic City. The partial blackout of that city has been ordered to provide safer passage of ships which would be silhouetted against the bright lights of the city.

I want to take this occasion to express my appreciation and that of the War Department for the splendid work that the American Medical Association is doing and will continue to do to aid the Army in the recruitment of physicians who are so badly needed.

Robert P. Patterson,
Under Secretary of War.

The Atlantic City hotels report many reservations; several leading hotels are already completely reserved. The program is complete, including several special sessions devoted to military medical problems. The Convention Number, giving full details, is scheduled for May 2.

MODERN BREAD

For some two years medical and nutritional scientists have discussed the nutritional significance of bread, lawyers have argued about regulations pertaining to flour and bread, advertising copy writers have written about the new enriched bread. Consumers apparently have continued to pay scant attention to the important changes that have been made recently in this basic food. The average American consumes each day about 6¼ ounces of white flour in various forms; to a large extent flour is used as white bread and other bakery products. This amount of flour will provide about one fourth of the average daily caloric requirements. The amount of white pan bakers' bread consumed daily is sufficient to provide each man, woman and child in the country with 70 Gm. of bread each day, or approximately two and one-third slices weighing 30 Gm. each. Nearly all this bread is consumed without special regard to its nutritional value.

Bread today is not the same as ordinary white bread of previous years. Now bakers use greater quantities of dried skim milk in the dough for all bread except Vienna style loaves. Rye bread and whole wheat bread also are ordinarily made without milk solids. If the skim milk solids are added at the rate of 6 pounds to each hundred pounds of flour (much of the white bread now is made with only half as much) the resulting white bread has almost the same riboflavin content as whole wheat bread made with water. Such milk bread has appreciably more calcium, from the milk solids, than the wheat grain. The milk proteins also represent a significant contribution. Nevertheless, ordinary white bread, while it is a good food, does not supply as much dietetic value as nutritional experts consider a bread should provide.

In a monograph entitled "Modern Bread from the Viewpoint of Nutrition," Sherman and Pearson [1] discuss the fundamental characteristics of bread as food, the individual nutritional essentials of importance in wheat and in bread, and the progress that has been made toward improving bread. Whole wheat, say Sherman and Pearson, is an excellent source of iron, but about four fifths of the iron of whole wheat is rejected in the milling of ordinary white flour. The grain is a good source of the vitamins of the B complex, especially of thiamine, but thiamine and riboflavin and nicotinic acid are largely lost in the milling of white flour. Recent work by Elvehjem, as yet unpublished, indicates that other factors of the vitamin B complex are rather uniformly distributed throughout the grain so that white flour and whole wheat flour are both fair sources of pantothenic acid and pyridoxine. Enriched bread will have a considerable portion of the original thiamine restored, and some of the nicotinic acid.

There are three principal methods by which a baker can make enriched bread. One is by using enriched flour instead of ordinary flour. Another is by incorporating in the dough a concentrate of either milling products of wheat or an artificial preparation of the desired composition. Another method is to use a yeast

1. Sherman, H. C., and Pearson, C. S.: Modern Bread from the Viewpoint of Nutrition, New York, Macmillan Company, 1942.

which has enhanced nutritive value. By any of these methods a white bread indistinguishable from ordinary white bread is obtained or it may have a light creamy color or yellowish brown. Nutritionally it is far superior to ordinary bread. Enriched bread does not have some of the disadvantages of whole wheat bread, although the latter is recognized as a meritorious product. The disadvantages overcome are the higher amount of roughage in whole wheat bread, which some persons are not able to tolerate, and the difficulty of keeping whole wheat flour.

The vast majority of Americans prefer white bread to dark bread. Enriched bread can be made to satisfy this wish without much sacrifice of nutritive values that are associated with the darker breads. In England nutritionally improved bread is made with flour of 85 per cent extraction,[2] meaning that only 15 per cent of the wheat grain is not incorporated in the flour. Ordinary white flour represents about 70 per cent extraction of the grain. The British bread is fortified with calcium salts, which is an optional ingredient of American enriched bread.

Each slice of either white, enriched or whole wheat bread will supply roughly about 15 Gm. of carbohydrate and 3 Gm. of protein, yielding about 70 calories. A slice of white bread will have about 0.02 mg. of thiamine, a slice of enriched bread will have about 0.07 mg., and a slice of whole wheat bread will have about 0.10 mg. of thiamine. Of nicotinic acid the amounts would be in each slice 0.2, 0.4 and 0.7 mg., the enriched bread again being intermediate in value between that of white bread and that of whole wheat bread. The iron content of the three products will be 0.1, 0.3 and 0.8 mg. respectively for a slice of white, enriched or whole wheat bread. These figures are based on the assumption that the enriched bread is of the minimum value that has been developed for this product. The tendency is definitely to aim toward the minimum rather than the maximum, which is four times more, or some intermediate value. Final standards for enriched bread have not yet been formulated by the Food and Drug Administration. It has been decided, however, that riboflavin, for which standards have been established for enriched flour, will not be required as an ingredient of that product until after the middle of the year 1942.

Within recent years all the changes and improvements in this product have been toward the improvement of its nutritive quality. In the development of enriched bread, bakers have been guided by leading scientists and medical investigators. Sherman and Pearson observe that enriched bread may now safely be utilized to supply as much as 40 per cent of the calories of the normal diet, provided the greater consumption of enriched bread is at the expense of less nourishing foods. This is an important observation—bread is exceptional from the point of view of economy. More than ever before bread deserves to be called the staff of life. Consumers who buy white bread should demand enriched bread.

[2] Specifications for National Flour, Nature **147**: 665 (May 31) 1941.

SYNTHESES IN THE INTESTINE

The manifold functions of the intestine create many practical problems for the physician. Not the least of these is the fact that the intestine is not sterile; probably the first swallow of food of the newborn infects the tract. The observation that the clotting time of the blood is reestablished at the normal level ordinarily within a week indicates that the intestinal bacterial activity involved in the synthesis of vitamin K is active at that time. Through this symbiotic activity, no doubt, the organism as a whole reaps benefits of various kinds from the biochemical reactions in the intestine. Vigorous support for this thesis has been adduced by some recent observations of synthetic activity in ruminants.

Although micro-organisms can flourish on nutrient mediums whose nitrogen is provided by such simple organic compounds as asparagin, succinamide and urea, only amino acid nitrogen, either as such or in the form of protein, will suffice to promote nutritive well being in the mammal. Nevertheless, in cattle and sheep, nitrogen balance and growth can be promoted when urea provides the major part of the nitrogen. Even the nitrogen of ammonium bicarbonate is utilized.[1] In recent investigations Harris and Mitchell[2] have demonstrated that urea added to a basal low protein ration not only decreases the loss of body protein of adult sheep but also improves the appetite and the digestibility of the other constituents of the diet. Furthermore, in studies on growing lambs it was shown that nearly normal growth is afforded by the nitrogen of the urea and that the increments of tissue growth are normal in chemical composition. Do these experimental results indicate that the ruminant has a strikingly different requirement for nitrogenous compounds than do man and the carnivora? The evidence indicates that the bacteria in the multiple pouched stomach of these types, utilizing the simple nitrogenous compounds provided in the experimental ration, synthesize their own cell protein and that this bacterial protein then becomes available for the nutrition of the host.

Synthetic activity of intestinal bacteria has been demonstrated in other directions. In a series of studies[3]

1. Hart, E. B.; Bohstedt, Gustav; Deubald, H. J., and Wegner, M. I.: J. Diary Sc. **22**: 785 (Oct.) 1939.
2. Harris, L. E., and Mitchell, H. H.: J. Nutrition **22**: 167, 183 (Aug.) 1941.
3. McElroy, L. W., and Goss, Harold: J. Nutrition **20**: 527, 541 (Dec.) 1940. Wegner, M. I.; Booth, A. N.; Elvehjem, C. A., and Hart, E. B.: Proc. Soc. Exper. Biol. & Med. **45**: 769 (Dec.) 1940; **47**: 90 (May) 1941. Hunt, C. H.; Kick, C. H.; Burroughs, E. W.; Bethke, R. M.; Schalk, A. F., and Gerlaugh, Paul: J. Nutrition **21**: 85 (Jan.) 1941.

on rumen contents of sheep and cattle secured either after slaughter or by means of a permanent fistula it has been demonstrated that the bacteria in the intestine are able to synthesize thiamine, riboflavin, pyridoxine, pantothenic acid and nicotinic acid as well as vitamin K. This formation of vitamins by intestinal bacteria, which occurred on natural feeds and on experimental rations, can be considered a more or less significant source of these indispensable factors to these animals.

Doubtless similar reactions take place in the human intestine, though the magnitude is too limited to be of practical significance. Nevertheless, such studies suggest that products of bacterial activity may play a part in instituting more favorable conditions in the intestine in man, such as follow implantation of Bacillus acidophilus. They may even play a part in immunity.

Current Comment

IMMUNIZATION IS 1942 MAY DAY OBJECTIVE

By authorization of an act of Congress, the President of the United States annually proclaims May Day, May 1, as Child Health Day. Usually special attention is given to the health of infants and children with special reference to preventive measures such as well baby supervision, immunization against communicable diseases, protection of the milk supply and water supply, and corrective measures relating to so-called physical defects. This year May Day is to have a special objective. The migration of populations as a result of defense and war industry, and the building of cantonments with consequent mushroom growth in surrounding communities, plus the necessity for being prepared for possible evacuation has emphasized the danger of epidemics of communicable diseases. The United States Children's Bureau, which is responsible for the May Day celebration, recommends that a major effort be made to secure at once the immunization of all children over 9 months of age against the two diseases for which established methods of immunization are available: smallpox and diphtheria. Instead of waiting for May Day, the Children's Bureau, under the Presidential proclamation, will call specifically for an immediate effort to immunize all children over 9 months of age and, as soon as possible after the ninth month, against these two diseases. Private physicians, public clinics, dispensaries and hospital outpatient departments are urged to make every effort to have these immunizations performed in all children touched by their respective services. This should be achieved before May 1 as a contribution to the health of the nation's children and as a wise precaution against possible epidemics which might go far to disrupt or slow war production or the training of soldiers. These diseases might spread from foci near camps and war industries into the industrial populations and the military and naval forces themselves. Adults, especially those not previously immunized against diphtheria, may be susceptible to these diseases, especially if they come from remote rural areas. In *Hygeia* in March there were published special articles on diphtheria immunization and smallpox vaccination, and many thousands of reprints are being distributed by health departments in various states. Although not specifically included in the May Day objective, immunization against typhoid, tetanus, whooping cough and scarlet fever may also be performed when indicated in the judgment of the physician.

"DOCTORS AT WORK" AUDIENCE CHECK

Radio program audiences can be checked in several ways. Audience mail response is one of the quickest and easiest, and, if interpreted conservatively, most satisfactory. Few programs receive audience mail in appreciable amount unless some effort is made to cause listeners to write. "Doctors at Work," the radio program of the American Medical Association and the National Broadcasting Company, now in its second season, has no product to offer for sale. To ascertain how many listeners would respond to an offer to send them printed material in the field of health education, Doctors at Work in January 1941 offered a list of first aid supplies and how to use them, suitable for pasting inside the medicine cabinet door. This was announced on two successive programs, only one short reference being made at the end of each broadcast. The offer brought 8,200 letters and cards requesting the list. In April, just as the touring season began to open, another test was made, this time of a chart and table of highway health and accident safeguards. This offer, made in the same way as that in January, brought only 2,800 replies. In 1940-1941, Doctors at Work enjoyed the advantage of a favorable evening hour, 10:30 p. m. eastern time, Wednesdays. In the 1941-1942 season a suitable evening hour was not available, and the series was opened on December 1 at 5:30 p. m. eastern time, Saturdays. In a few weeks this time was switched to 5 o'clock eastern time, where it has since remained. In March 1942 an offer was made to listeners to send them a check list of fifty factors which contribute to the health of home and family, an instrument by which their own health practices could be evaluated. The offer was made in the usual fashion, one short reference on two successive broadcasts. The number of replies exceeded 8,600 (8,650, March 31). It is, of course, impossible to estimate accurately the actual number of listeners from such responses. However, only small percentages of listeners respond even to an offer of more or less tangible objects, such as usable samples. The responses to audience mail tests here reported are considered in radio circles highly satisfactory for a noncommercial program. Doctors at Work has a large following of faithful listeners. This following is nationwide; every state is represented in this response, as are Canadian listeners.

MEDICINE AND THE WAR

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medicine and the war, and such other information and announcements as will be useful to the medical profession.

PROCUREMENT AND ASSIGNMENT SERVICE FOR PHYSICIANS, DENTISTS AND VETERINARIANS

CIVIL SERVICE COMMISSION RECOMMENDS ENROLMENT

In the past, the U. S. Civil Service Commission, in furnishing to federal agencies the names of physicians, dentists and veterinarians who had qualified in civil service examinations, has found that the making of appointments has been retarded by an excessive proportion of declinations from those eligible when appointment was offered. Persons who were available for federal medical positions when the examination was held were no longer available for such appointment when their names were reached on the commission's register of the eligible.

The present war emergency demands promptness in filling vacancies in various governmental agencies, and the determination of immediate availability of applicants for civil service employment early in the examining process has become of increasing importance. The U. S. Civil Service Commission, therefore, is recommending that all physicians, dentists and veterinarians who are interested in civil service employment enrol with the Procurement and Assignment service, and that they definitely indicate on the questionnaire the governmental agency in which they desire employment.

The agencies which employ the largest number of physicians and dentists under civil service regulations are the Veterans Administration, the Indian Service (Department of the Interior), the Public Health Service (Federal Security Agency), the Panama Canal and the Children's Bureau (Department of Labor).

At present there is a shortage of fully qualified physicians who are available for employment in the federal civil service, and it is important that more of the physicians who are not available or qualified for commissions in the Army, Navy or Public Health Service offer their services during the war emergency in a civilian capacity in federal agencies having civilian medical services.

In accordance with an executive order, "war service" appointments are now being made in the various governmental agencies. Such appointments are for the duration of the war and for six months thereafter. The physical requirements for war service appointments are liberal. Appointments are being made of physicians who qualify for the associate or full grade medical officer under the U. S. Civil Service Commission's current open continuous examination. To qualify as the associate or full grade medical officer, physicians must have graduated from an approved medical school subsequent to May 1, 1920.

The U. S. Civil Service Commission will utilize the information obtained by the Procurement and Assignment Services's enrolment program in recruiting physicians, dentists and veterinarians to fill the needs of the civilian medical, dental and veterinarian services of governmental agencies.

VERNE K. HARVEY, M.D., Washington, D. C.
Medical Director, U. S. Civil Service Commission.

FEDERAL CIVIL SERVICE

VERNE K. HARVEY, M.D.,
Washington, D. C.

The U. S. Civil Service Commission, responsible for the recruitment of medical and other personnel for positions in the federal government which are subject to civil service law, joins other federal agencies in urging physicians, dentists and veterinarians to enroll with the Procurement and Assignment Service when the enrolment forms are mailed in the very near future.

The commission emphasizes that the lists compiled through the enrolment will be utilized in filling not only positions in the commissioned medical services of the War and Navy departments and the Public Health Service but positions in civilian medical services of federal agencies as well.

The commission is continuing to recruit medical officers by the direct method of announcing and publicizing examinations for medical positions. An examination for medical officer, for example, has been announced on a "continuously open" basis. But the demands of the federal agencies, rapidly expanding as a result of the national emergency, cannot be met by this method alone.

As a supplementary measure, therefore, the commission will call for the names of qualified persons appearing on lists of the Procurement and Assignment Service who have indicated in their enrolment forms that they are interested in serving in a civilian capacity in one of the federal agencies. The Procurement and Assignment Service will give due consideration to whatever other requests for personnel are pending and then furnish to the commission the names of available physicians, dentists or veterinarians. The Procurement and Assignment Service would select the names of (*a*) persons who had indicated in their enrolment forms that they were primarily interested in positions in the federal civil service and (*b*) persons who had expressed a preference for positions in the commissioned service of the War or Navy Department or the Public Health Service but were not qualified therefor. In either instance, only those persons who met the requirements of the commission's examination would be certified to an agency for appointment.

ENROLMENT

Physicians, dentists and veterinarians are requested to indicate in spaces provided on the enrolment form in which of the following classes of medical service they prefer to assist: (1) military (commissioned services of the War and Navy departments and the Public Health Service), (2) governmental (civil service), (3) industrial and (4) civil (nongovernmental). They should indicate their first, second, third and fourth preferences.

Under the heading "U. S. Civil Service Agencies" is a list of some of the federal agencies which maintain civilian medical

services. Those who are interested in employment in the federal civil service should indicate the agency in which they prefer to serve.

PROCEDURE IN MAKING RECOMMENDATIONS

In recognition of the Procurement and Assignment Service's role as the central agency coordinating the distribution of medical personnel, the Civil Service Commission will proceed as follows when applications are received in response to announcement of civil service examinations for physicians, dentists and veterinarians:

1. The names of those applicants who have received an eligible rating will be submitted to the Procurement and Assignment Service, with the view of determining whether or not such applicants are essential in their present positions and localities.

4. The names of those persons who have been designated by the Procurement and Assignment Service as being essential in their present positions and localities will not be certified, and such persons will be notified by the United States Civil Service Commission that they cannot be certified in view of the action taken by the Procurement and Assignment Service.

3. The names of those persons who have been designated as available will be certified as candidates to fill the personnel needs of the various government agencies under civil service rules and regulations.

POSITIONS NOW OPEN IN CIVIL SERVICE

Under an executive order which became effective March 16, 1942 appointments to positions in the federal civil service (those positions in the federal executive civil service which are subject to the Civil Service Act) are placed on a "war service" basis. Appointments are made with the understanding that, provided satisfactory service is rendered, tenure will be for the duration of war and for six months thereafter. Probationary, or "permanent," appointments have been discontinued "for the duration."

Civil service examinations are now open for associate medical officer, $3,200 a year; medical officer, $3,800, and senior medical officer, $4,600. No written test is required. Determination as to whether an applicant is eligible or ineligible for appointment is made on the basis of his education and experience. Applications are considered for any of fifteen optional branches of medical science. Full information regarding the medical officer examinations is set forth in a printed announcement which may be consulted at any first or second class post office. Copies may be obtained by writing to the U. S. Civil Service Commission, Washington, D. C.

A diversified field is open to the physician who elects to assist in the civilian medical services of the federal government during the emergency. The field encompasses virtually every phase of medical activity, ranging from rural practice to the most highly specialized activities.

THE INDIAN SERVICE

Not all civil service physicians are employed in large government hospitals. Many—for example, those employed in the Indian Service—are engaged in the general practice of medicine. The Indian Service maintains general hospitals and sanatoriums ranging from fifty to two hundred and fifty beds. Very active outpatient departments are connected with these hospitals. The physicians make home calls and field trips, conduct school examinations and administer general public health measures among the Indians.

PANAMA CANAL ZONE

Physicians who are interested in tropical diseases receive excellent opportunities to study that subject in the Canal Zone. Civil service physicians in the Canal Zone are employed primarily in dispensary and quarantine work. The dispensary work consists of general practice involving the attendance of government employees and their families, and crews and passengers of vessels. Quarantine physicians are concerned with quarantine and immigration inspection of crews and passengers on incoming vessels.

VETERANS ADMINISTRATION—SPECIAL SERVICES

Large numbers of federal medical officers are engaged in the fields of general practice, tuberculosis, psychiatry, surgery and public health. The opportunity for research in these fields is excellent. The Veterans Administration operates a large tumor clinic at Hines, Ill., tuberculosis clinics at the tuberculosis hospitals, and heart clinics at Mount Alto Hospital, Washington, D. C. At St. Elizabeths Hospital, Washington, D. C., fine opportunities for residencies and internships in neuropsychiatry are open to recent graduates of medical schools. This hospital is under the jurisdiction of the Federal Security Agency.

FOOD AND DRUG ADMINISTRATION

Medical officers in the Food and Drug Administration (Federal Security Agency) are engaged in a critical review of the labelings of medicines in the light of their composition for the purpose of ascertaining whether or not the therapeutic representations are true or false as judged by a consensus of present day medical opinion. This work offers excellent opportunities to recent graduates of medical schools who have had, in addition to their regular medical education, experience in pharmacology.

CHILDREN'S BUREAU

The Child Hygiene Division of the Children's Bureau (Department of Labor) carries on research and investigation involving fundamental technical medical investigations of the mental and physical condition of children in relation to heredity, environment, nutrition and the efficacy of various methods of community health work. There are opportunities in this bureau for physicians with special training in pediatrics, obstetrics or public health procedure.

PUBLIC HEALTH SERVICE

Civilian medical officers in the Public Health Service (Federal Security Agency), as distinguished from medical officers in the commissioned force, are appointed as acting assistant surgeons and are usually detailed for local duty in the vicinity in which they reside. From time to time, however, there is opportunity for them to transfer elsewhere. They are employed in connection with practically all the activities of the Public Health Service. These include hospital and relief work, quarantine and immigration work, field investigations and epidemic control duty. The Public Health Service operates marine hospitals and relief stations throughout the United States. The beneficiaries in these hospitals and relief stations consist principally of merchant seamen, officers and enlisted men of the United States Coast Guard and civil employees of the federal government injured in line of duty.

The services of acting assistant surgeons are utilized at a large number of marine quarantine stations in connection with the inspection of vessels entering the United States from foreign ports and in connection with the medical examination of aliens entering this country. Acting assistant surgeons conduct investigations pertaining to industrial hygiene, goiter, anthrax, influenza, malaria, pellagra, pneumonia, tuberculosis, typhoid, child hygiene and public health administration.

VETERANS ADMINISTRATION

The Veterans Administration employs more civil service physicians than any other government agency. The medical service of the Veterans Administration comprises regional offices, facilities and diagnostic centers. The term "facility" is applied to various types of field stations, including those which are hospitals only, those which may provide domiciliary care and hospitalization, others which are a combination of regional offices and hospitals, and still others which are a combination of regional offices and homes. Facilities may be primarily designed for general (medical and surgical) service or for tuberculosis or neuropsychiatric service. However, some have a mixed service which may be a combination of any of these.

New appointees are first sent to one of several selected facilities of the Veterans Administration, at which they are given a training course in medical subjects and in administration, as based on the Regulation and Procedure, the Manual for Medical Examiners, clinical bulletins and other instructional publications of the Veterans Administration. After passing an examination at the end of this preliminary training course, appointees are assigned at the same or another facility for ward and other duties pertaining to an associate physician. Physicians in the service must be available for transfer to any facility within the continental limits of the country as need for their service arises.

The diagnostic centers located at Washington, D. C., Hines, Ill., and San Francisco were established for intensive study and

observation of patients presenting diagnostic problems and have consultant staffs consisting of physicians of national reputation in their fields. The diagnostic center at Hines, Ill., has one of the largest and most modern tumor clinics in the world.

Small clinics for thorough diagnosis and treatment of malignant growths are located strategically in facilities in New York City, Washington, D. C., Atlanta, Ga., Portland, Ore., and Los Angeles.

In nine facilities, scattered throughout the country, centers have been created for special chest surgery.

The volume and variety of the medical activities of the Veterans Administration are approached by few if any other organization. Veterans of former wars constitute a public of approximately four and one-half million persons who are potentially entitled to treatment by the Veterans Administration. Continuous accretions to that total are made through discharges from service of disabled officers and enlisted men of the Army, Navy, Marine Corps and Coast Guard. The huge total of hospital beds is constantly in demand, and abundant clinical material is afforded in all fields of medicine save obstetrics and pediatrics. The proportions of outpatient activities are unprecedented: In the fiscal year ended June 30, 1941 a total of 1,111,589 physical examinations were made and 1,176,658 treatments were rendered in the outpatient service. It is not only the numerical proportions of this service that make it valuable but quite as much the peculiar advantage derived from the continuity of contact that is afforded. It is the usual experience of civilian clinics to have patients drop off before completion of study or treatment; but the reexaminations that are called for from time to time, for purposes of pension, disability, compensation, government insurance, treatment and so on insure follow-up of Veterans Administration beneficiaries through successive years. The evolution of conditions can thus be observed, errors in earlier diagnoses can be corrected, and treatment to meet present indications can be prescribed to advantage through these circumstances.

The Veterans Administration is committed to and maintains a high standard of medical treatment and care. Clinicopathologic conferences of hospital staffs are regularly held. Continuous attention is given to the introduction of new diagnostic and treatment methods, and the laboratory and clinical equipment is of modern design. Postgraduate "refresher" courses, as well as postgraduate courses in the specialties, are arranged whenever necessary at several of the larger stations, and official leave may be granted for attendance at courses in other clinics and hospitals in the country.

Medical research is supervised by a specially trained physician of the staff of the medical director, and projects are entrusted to physicians having the basic special qualifications to conduct them or who show aptitude for research. The Cardiovascular Research Unit, at Washington, D. C., was organized, under the direction of a chief, to standardize concepts and practices in cardiology, use of the electrocardiograph and so on. The Tumor Research Unit at Hines, Ill., conducts clinical and experimental research into the cancer problem and has published numerous papers and monographs on technical phases of this work. The Neuropsychiatric Research Unit at Northport, L. I., N. Y., conducts clinical and laboratory research in connection with neuropsychiatric disabilities and is engaged in standardizing the diagnostic and therapeutic methods used in connection with the management of neuropsychiatric disabilities. The *Medical Bulletin* of the Veterans Administration, issued quarterly, provides opportunity for the publication of articles and case reports prepared by physicians of the service.

OTHER GOVERNMENT AGENCIES

To a lesser extent, medical officers are employed in various other government agencies. Two medical officers in the Government Printing Office are in charge of a small well equipped hospital in which employees who are injured or become ill while on duty are treated. The Bureau of Engraving and Printing requires the services of a physician for similar duty. The Census Bureau of the Department of Commerce employs physicians who engage in medical statistical study. In the Civil Service Commission in Washington, D. C., and in thirteen district offices a number of medical officers are engaged in medical activities pertaining to government employment. This activity is a combination of insurance, industrial and administrative medicine and affords young physicians a basic training in these fields which is unique in the United States.

HEALTH OF SELECTIVE SERVICE REGISTRANTS

LEONARD GEORGE ROWNTREE, M.D.
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KENNETH H. McGILL, A.B.
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and
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Captain, U. S. Army; Chief, Medical Statistics Section Research and Statistics Division
Washington, D. C.

The Selective Service System is making a comprehensive analysis of the reports of physical examination of the registrants examined in accordance with the Selective Training and Service Act of 1940. Pending the complete analysis of these reports, a survey has been made of 19,923 medical records to provide an index to the physical fitness for military service of American youths between the ages of 21 and 36. This sample was drawn from each state in proportion to total registration and consists of a cross section of registrants examined prior to May 31, 1941.

RATE AND CAUSES OF REJECTION

This sample analysis of medical records and summary reports from the Selective Service local boards indicates that about 50 per cent of the approximately two million registrants who have been examined have been found by local boards and by Army induction stations to be unqualified for general military service, physically, mentally and educationally. Of the approximately one million registrants who were not qualified for general military service, 900,000 were so classified because of lack of physical and mental qualifications and the remaining 100,000 because of lack of educational qualifications. The minimum educational requirement for a registrant to be inducted into the Army is the ability to read and write the English language as well as a student who has satisfactorily completed the fourth grade in an American grammar school. More than one half, 470,000, of the 900,000 rejected for physical and mental reasons were qualified for limited military service only, and 430,000 were totally disqualified for any military service.

Based on the major pathologic condition recorded or the principal cause of rejection by Selective Service local boards and by Army induction stations, dental deficiencies accounted for an estimated 188,000, or 20.9 per cent of the 900,000 registrants not qualified for general military service. Defects of the eyes and impaired vision constituted an estimated 123,000, or 13.7 per cent.

The estimated number of registrants found to be unqualified for general military service by other defects or diseases are set forth in table 1 and chart 1. The table also shows a breakdown of the number who were found to be available for limited military service by Selective Service local boards and those who were dis-

qualified for any military service. Hernias, venereal diseases and defects and diseases of the teeth, eyes and feet were the principal types that, while disqualifying for general military service, still would permit the individual registrant to perform limited military service. Diseases and defects of the cardiovascular system seem to be the principal causes in total disqualifications for any military service.

Included in the miscellaneous group were diseases and defects of the mouth and gums, nose, throat, kidneys and urinary system, abdomen, genitalia and skin together with hemorrhoids, varicose veins, tumors, and infectious and parasitic diseases.

INCIDENCE OF DEFECTS

The major pathologic condition indicates the reason why registrants were rejected but does not afford an accurate index as to the incidence and prevalence of diseases and defects among registrants. In this study a maximum of three defects was recorded. A total of 27,031 defects were tabulated from the 19,923 reports of physical examination, an average of one and four-tenths defects per registrant examined. No defects were recorded, however, for 5,741 registrants, or 29 per cent, of the total number examined. Of the total of 27,031 defects, one or more were recorded for each of 14,182 registrants, an average of one and nine-tenths defects per registrant with defects. Two defects were recorded for each of 8,433 registrants and three defects for 4,416 registrants.

In table 2 there is a list of the defects or diseases tabulated by broad classifications with the rate per thousand registrants examined. This tabulation includes defects which do not disqualify as well as defects which do disqualify for general military service. Defective feet accounted for the largest number of disease and defects recorded for any single organ, section or system of the body and comprised 10.7 per cent of the total number of defects tabulated. Dental defects, which were the largest cause of rejection for military service, comprised 10.3 per cent of the diseases and defects. In addition to nondisqualifying defects, a large proportion of the disqualifying defects are minor as far as health conditions are concerned.

Many defects are a cause for rejection for service in the Army but in no way hinder the performance of many civilian occupations.

AGE, HEIGHT AND WEIGHT OF REGISTRANTS

As the reports of physical examination considered in this survey were for men examined prior to May 31, 1941, registrants between the ages of 21 and 36 were included as well as a small number of men between the ages of 18 and 21 who volunteered through the Selective Service System for military service. Two thirds of the registrants examined by local boards were between the ages of 21 and 27, inclusive. Registrants between the ages of 28 and 36, inclusive, accounted for 31.3 per cent of the total number examined, and the number of volunteers between the ages of 18 and 21 accounted for 2.1 per cent of the total registrants examined.

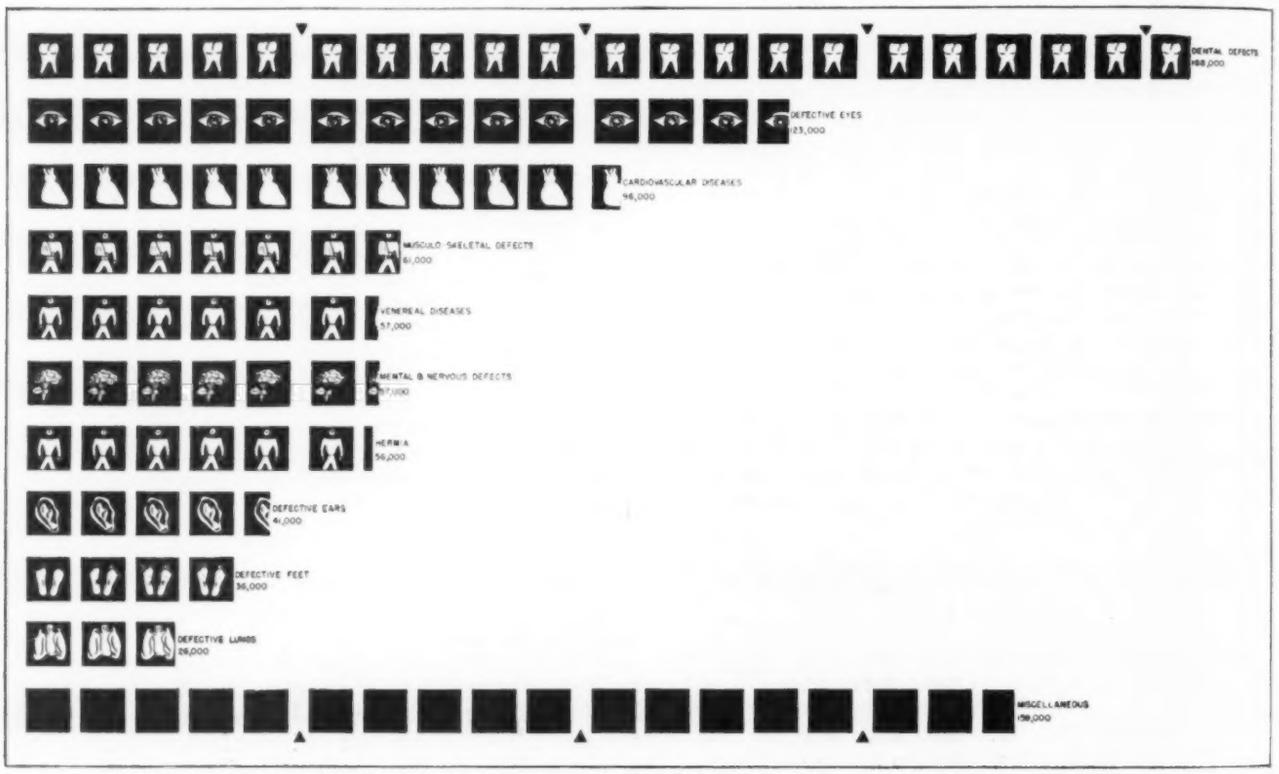


Chart 1.—Estimated number of selectees rejected. Each symbol represents 1 per cent of the 900,000 rejected.

The rate of rejection for registrants between the ages of 31 and 36 was nearly twice as great as that of registrants between the ages of 21 and 25, inclusive. Sixty-one per cent of the registrants between the ages of 31 and 36 were unacceptable for general military service as compared to 45 per cent between the ages of 26 and 30 and 34 per cent between the ages of 21 and 25. The percentage who were qualified for general military service varied from 70.5 for registrants 21 years old to 29.9 for registrants who were 36 years old at the time of physical examination.

The relationship that exists between the registrants' age and availability for general military service is shown in table 3 and chart 2.

The average height of registrants examined was 67½ inches (171 cm.), the average weight was 150 pounds (68 Kg.) and the average chest measurement in forced expiration was 33 9/10 inches (86 cm.). The average height of registrants qualified for general military service was 68 1/10 inches (173 cm.) and the average weight was 152 pounds (69 Kg.). The height of registrants examined varied from 54 inches (137 cm.) to 88 inches (223.5 cm.), and 98.3 per cent of the registrants were between 60 inches (152 cm.) and 78 inches (198 cm.) in height, which are the minimal and maximal heights, respectively, for acceptance by the Army.

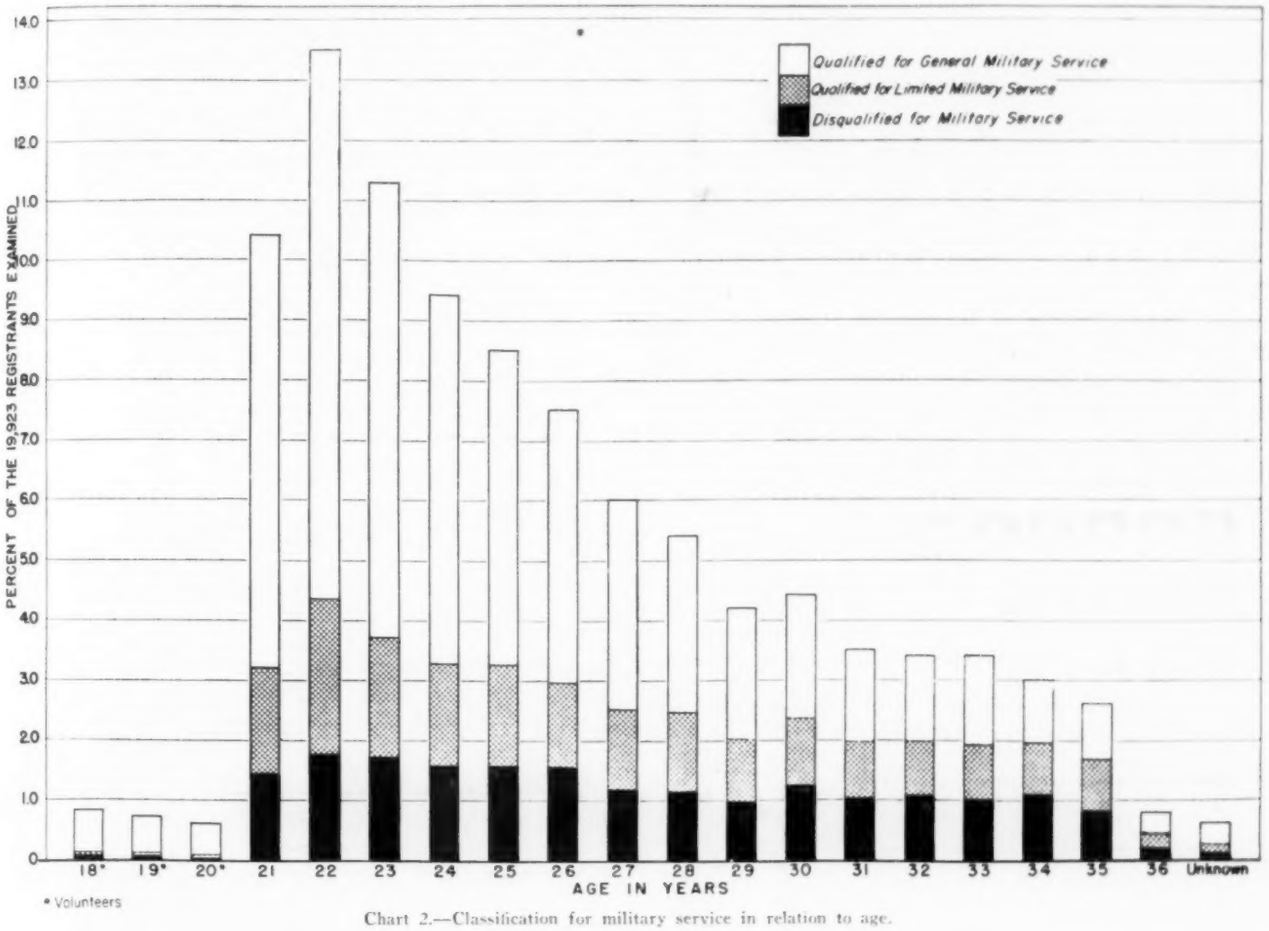


Chart 2.—Classification for military service in relation to age.

Registrants varied in weight from 85 pounds (38.6 Kg.) to 385 pounds (175 Kg.), and 93 per cent were between 100 pounds (45.4 Kg.) and 190 pounds (86 Kg.). The minimum weight for admittance into the Army for registrants 60 inches (152 cm.) tall is 105 pounds (47.6 Kg.), and the standard weight for a registrant 78 inches (198 cm.) tall is 184 pounds (83.5 Kg.).

RACE, URBAN-RURAL RESIDENCE AND PLACE OF BIRTH

The ratio of Negro registrants to the total number examined was approximately the same as the ratio of Negroes to the total population, 11 per cent. Registrants of other races, which accounted for less than 1 per cent of the total number examined, were mostly Chinese, Japanese and Indians. The rate of rejection for Negro registrants was 42.6 per cent as compared to 40.8 per cent for white registrants. Two thirds of the registrants examined were from urban communities. The rate of rejection for registrants from urban areas was 42.4 per cent as compared to 38.1 per cent for rural areas.

The United States and its territories were the place of birth of 97.3 per cent of the registrants examined, most of the others having been born in Canada, British Isles and Europe. The rate of rejections for native born registrants was 40.9 per cent as compared to 45.6 per cent for registrants who were born outside the United States and its territories.

This finding perhaps, can be accounted for by the differences in age groups.

OCCUPATION

About one seventh of all registrants examined were unemployed at the time of examination. The largest group of employed registrants physically examined were operatives and kindred workers, which comprised about 20 per cent. Most numerous among operatives and kindred workers were chauffeurs, truck drivers, delivery men, weavers, knitters, spinners, assemblers and operators of lathes, drill presses and other machines. Farmers and farm laborers, the second largest employed group, accounted for 14 per cent of the total number examined. Craftsmen and foremen, which acounted for 8 per cent of all registrants examined, were mostly carpenters, cabinet makers, pattern makers, mechanics, repairmen, machinists, millwrights, tool makers, painters, paper hangers and printers. Approximately 1 per cent of the registrants examined were students. The occupations of the registrants examined are shown by broad classifications in table 4.

COMMENT

The information and data contained herein are the best available as to the health of a part of the United States male population. While these data indicate that approximately one half of the registrants being examined are found to be unfit for the performance of general military service, an additional one fourth are qualified for limited military service. Registrants classed as available for limited military service are not being inducted at the present time.

There seems to be little doubt that most of the registrants classed as available for limited military service and a substantial portion of those classed as disqualified for any military service in the United States Army evidence health conditions which would be acceptable for military duty in any army in continental Europe. Registrants are not physically examined who are found by Selective Service local boards to be essential to the national health, safety and welfare, such as those having community responsibilities to dependents or holding essential jobs.

In the World War approximately 64 per cent of the 3,208,446 registrants examined between Dec. 15, 1917 and Sept. 11, 1918 were qualified for general military service.[1] An additional 17 per cent were qualified for limited military service, and 19 per cent were disqualified for any type of military service. This compares, not so unfavorably, with about 25 per cent being totally rejected for any type of military service at the present time when it is recalled that the examinations were made under considerably different conditions. During the World War period standards changed seven times. Registrants being examined during that period were mostly between the ages of 21 and 30 as compared to 21 and 36 in the data presented here.

Advances since 1918 in clinical medicine and diagnostic and laboratory procedures now present the means of eliminating more men from the service. For example, many registrants are being rejected because of latent syphilis that would not have been recognized in the World War. Chest roentgenograms are being used extensively. Many cases of tuberculosis are being found now that could not previously have been detected. By concentrated efforts, many of the men with borderline mental conditions are being rejected at the present time who would have been accepted into the Army in 1918. Also the psychology of the examiners themselves is entirely different than that which prevailed in the World War. Then it was necessary to secure men quickly, train them hurriedly and transport them to the theater of operation in the minimal time possible. Hurried examinations did not permit the close observations that are being made today. It is essential for the men being inducted into the Army at the present time to be capable of efficient work and hard living, and to

TABLE 1.—*Estimated Number of Registrants Found to be Unqualified for General Military Service Because of Physical and Mental Reasons, by Availability for Military Service and by Defect or Disease*

Major Defect or Disease	Unqualified for General Military Service by Selective Service *			Unqualified for General Military Service by the Army †	Total Unqualified for General Military Service	Percentage of Estimated Total Unqualified for General Military Service
	Qualified for Limited Military Service	Disqualified for Any Military Service	Total			
Teeth	100,000	53,000	153,000	35,000	188,000	20.9
Eyes	72,000	28,000	100,000	23,000	123,000	13.7
Cardiovascular system	17,000	67,000	84,000	12,000	96,000	10.6
Musculoskeletal	27,000	25,000	52,000	9,000	61,000	6.8
Venereal	35,000	14,000	49,000	8,000	57,000	6.3
Mental and nervous	8,000	30,000	38,000	19,000	57,000	6.3
Hernia	35,000	11,000	46,000	10,000	56,000	6.2
Ears	7,000	18,000	25,000	16,000	41,000	4.6
Feet	21,000	9,000	30,000	6,000	36,000	4.0
Lungs ‡	6,000	11,000	17,000	9,000	26,000	2.9
Miscellaneous	72,000	54,000	126,000	33,000	159,000	17.7
Total	400,000	320,000	720,000	180,000	900,000	100.0

* The major defect or disease for each registrant was determined by the principal cause of rejection.

† These estimates are based on classification reports from local boards as to the number qualified for limited military service, the number disqualified for any military service, and on the rates of rejection for each group of defects or diseases as revealed in an analysis of 19,923 reports of physical examination. These estimates are based on the classification reports from local boards as to the total number found unqualified for general military service at the Army induction station, and on the rates of rejection for each group of defects or diseases as revealed in an analysis of 123,000 reports of physical examination at the Army induction station as released by the War Department.

‡ Including tuberculosis.

TABLE 2.—*Incidence of Defects Found in 19,923 Registrants Examined by Selective Service Local Boards*

Defect or Disease	Number of Defects Found	Rate of Defects per 1,000 Examined
Eyes	2,305	115.7
Ears	887	44.5
Teeth	2,795	140.3
Mouth and gums	1,273	63.9
Nose	1,372	68.9
Throat	1,321	66.3
Lungs	327	16.4
Tuberculosis	114	5.7
Cardiovascular system	2,000	100.4
Blood and blood-forming organs	19	1.0
Hernia	1,287	64.6
Kidneys and urinary system	279	14.0
Abdominal viscera	244	12.2
Genitalia	1,175	59.0
Venereal	695	34.9
Skin	2,308	115.8
Hemorrhoids and rectal defects	610	30.6
Varicose veins	531	26.7
Mental and educational deficiency and illiteracy	239	12.0
Mental disorders	362	18.2
Neurologic	454	22.8
Musculoskeletal	2,018	101.3
Feet	2,888	145.0
Endocrine disturbances	319	16.0
Tumors	228	11.3
Infectious, parasitic and epidemic diseases	7	0.4
Other diseases and defects	974	48.9
Total	27,031	1,356.8

TABLE 3.—*Age of Registrants by Availability for Military Service*

Age *	Total Examined		Qualified for General Military Service		Qualified for Limited Military Service		Disqualified for Military Service	
	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent
18	153	0.8	129	84.3	8	5.2	16	10.5
19	143	0.7	118	82.5	13	9.1	12	8.4
20	127	0.6	94	74.0	17	13.4	16	12.6
21	2,083	10.4	1,469	70.5	347	16.7	267	12.8
22	2,688	13.5	1,810	67.3	511	19.0	367	13.7
23	2,248	11.3	1,504	66.9	393	17.5	351	15.6
24	1,872	9.4	1,222	65.3	343	18.3	307	16.4
25	1,692	8.5	1,034	61.1	331	19.6	327	19.3
26	1,492	7.5	905	60.7	276	18.5	311	20.8
27	1,189	6.0	682	57.4	268	22.5	239	20.1
28	1,071	5.4	576	53.8	260	24.3	235	21.9
29	839	4.2	435	51.8	213	25.4	191	22.8
30	869	4.4	400	46.0	226	26.0	243	28.0
31	697	3.5	306	43.9	188	27.0	203	29.1
32	681	3.4	282	41.4	188	27.6	211	31.0
33	669	3.4	282	42.4	188	28.1	199	29.7
34	602	3.0	212	35.2	159	26.4	231	38.4
35	527	2.6	176	33.4	172	32.6	179	34.0
36	157	0.8	47	29.9	54	34.4	56	35.7
Unknown	124	0.6	71	57.2	29	23.4	24	19.4
Total	19,923	100.0	11,754	59.0	4,184	21.0	3,985	20.0

* Age at last birthday at time of physical examination.

1. Second Report of the Provost Marshal General to the Secretary of War on the Operations of the Selective Service System to Dec. 20, 1918, Washington, D. C., Government Printing Office, 1919.

be otherwise capable of handling the more complicated procedure and mechanics of the modernized army.

The average height of recruits examined during the World War was 67½ inches (171 cm.), the average weight was 142 pounds (64 Kg.) and the average chest measurement in forced expiration was 33⅕ inches (84 cm.). It is estimated that the average height in men examined for military service in the federal forces during the Civil War was 67½ inches (171 cm.), the average weight was 136 pounds (61.7 Kg.) and the average chest measurement at expiration was 33½ inches (84 cm.).[2] In Canada the average height of registrants being examined for military duty is 66⅔ inches (169 cm.), the average weight 144⅔ pounds (65.5 Kg.) and the average age 22½ years. Comparison of defects with those found in men entering the Canadian army is not possible, owing to the fact that the examination given is primarily a coarse screening as compared to the thorough examination in this country. The principal causes of rejection in Canada are defects of the feet and nose, and hernias.

TABLE 4.—*Occupations of 19,923 Registrants Physically Examined*

Occupation	Number of Registrants Physically Examined	Percentage of Total Examined
Professional workers	590	3.0
Semiprofessional workers	226	1.1
Farmers (owners, tenants and croppers) and farm managers	1,099	5.5
Proprietors, managers and officials, except farm	779	3.9
Clerical and kindred workers	1,548	7.8
Salesmen	878	4.4
Craftsmen, foremen and kindred workers	1,679	8.4
Operatives and kindred workers	4,064	20.4
Domestic service workers	56	0.3
Protective service workers	64	0.3
Service workers, except domestic and protective	936	4.7
Farm laborers and foremen	1,683	8.4
Laborers, except farm and mine	2,487	12.5
Nonclassifiable returns	571	2.9
Emergency workers and unemployed	3,042	15.3
Students	221	1.1
Total	19,923	100.0

The administration by the Selective Service System and the Army of what might be considered fairly high physical standards has produced, unqualifiedly, an army with the best physical condition of any comparable sized army in history. In many cases such modern conveniences as automobiles, street cars, elevators and household gadgets have produced flabbiness of muscle and at times paunchiness in the waistline. This, however, is not to be confused with soundness of health, which is determined more by sturdiness of framework, a sound heart, sound lungs and respiratory system, a good digestive system and a stable mental and nervous system. The vast majority of registrants can be hardened by training. This does not mean, however, that we should overlook the warning signaled to us by the discovery of this huge number of hidden defects and diseases in such a large proportion of the registrants.

2. Medical Department of the United States Army in the World War, Volume XV, Statistics, Part I, Army Anthropology, Charles B. Davenport and Albert G. Love, Washington, D. C., Government Printing Office, 1921.

SPECIALISTS SHARE FEES WITH MEMBERS IN MILITARY SERVICE

Recognizing the financial sacrifice which members of its organization who have gone into the military service have made, the Indianapolis Ophthalmological and Oto-Laryngological Society has adopted a resolution to the effect that 50 per cent of all fees collected by members from patients who belong to the practice of any member engaged in military service shall be remitted to such members until they return to civil practice; also that on return from military service to civil practice of such members, all patients belonging to their prior practice shall be returned to them by those members who may come into professional contact with such patients. The society also voted to waive all dues and assessments of those who enter the military service and shall consider such members in good standing in that society for the duration of their military service and for the period of one year thereafter.

FUNCTION OF MEDICAL ADVISORY BOARDS (VI)

Memorandum (1-403) Concerning Relationships of Medical Examinations by Induction and Advisory Boards

It has been brought to the attention of this headquarters that in some of the corps areas registrants are being referred back to local boards and medical advisory boards by the examining and induction stations for additional examinations, including laboratory and x-ray tests, to determine their physical qualifications for induction.

The Medical Advisory Board is an element of the Selective Service System. There is no objection to the use by the Army of the specialists on such boards provided the cost is borne by the Army and it is distinctly understood that such services are rendered to and for the Army. In no event should a registrant be referred back to local boards for an additional examination prior to a final action by the examining and induction stations.

A problem arises, not infrequently, at the examining and induction stations, where the registrant declares that he suffers from epilepsy, asthma or other conditions and yet presents no proof other than his bare statement. Because of lack of acquaintance with the registrant, the examiner naturally is uncertain as to the truth or falsity of the statement. If such cases are rejected and returned to the local board, a statement will be made by the examining and induction stations under remarks on the "Report of Physical Examination and Induction" (form 221), giving the basis for the cause of rejection. If the local board or its examining physician has reason to believe that the registrant has falsified such a statement, it may accumulate evidence to justify its belief and return the registrant at a subsequent date, accompanied by such evidence.

LEWIS B. HERSHEY,
Director, Selective Service System.

PRICE OF RUBBER DRUG SUNDRIES

Manufacturers of rubber drug sundries, including essential hospital and medical items, were requested not to advance prices above those in effect on March 1 in a letter sent to them by Acting Price Administrator John E. Hamm of the Office of Price Administration. The purpose of the request is to keep prices from mounting pending completion of an investigation to determine proper maximum prices for rubber drug sundries. Manufacturers of such items have been allotted a supply of crude rubber and latex by the War Production Board because of the essential nature of the products. It is "essential that prices at all manufacturing and distributing levels reflect only increases which are absolutely necessary for the maintenance of production." Manufacturers will be asked in the near future to submit pertinent cost and earnings data. Manufacturers who intend any change in specifications or quality standards are asked to communicate with the OPA before establishing prices on the altered articles.

NEW ARMY DENTAL CHIEF

Col. Robert H. Mills, D. C., U. S. Army, has been nominated by the President to be Assistant Surgeon General, to succeed Brig. Gen. Leigh C. Fairbank, D. C., who retired on February 28. Colonel Mills has been chief dental surgeon in the Ninth Corps Area.

ORGANIZATION SECTION

OFFICIAL NOTES

INDUSTRIAL HEALTH

Report of a Joint Session Between the Subcommittee on Industrial Health and Medicine, Federal Security Agency, and the Council on Industrial Health, American Medical Association

The Subcommittee on Industrial Health and Medicine of the Federal Security Agency and the Council on Industrial Health met jointly in Chicago on Sunday, January 11. Those present were Stanley J. Seeger, Harvey Bartle, Leverett D. Bristol, Warren F. Draper, Philip Drinker, Leroy U. Gardner, Raymond Hussey, Anthony J. Lanza, Robert T. Legge, Clarence D. Selby, Roscoe L. Sensenich, Olin West, Carl M. Peterson, James A. Crabtree, E. C. Holmblad, Lloyd Noland, George M. Smith, Capt. T. C. Bedwell, J. J. Bloomfield, Lieut. Comdr. Otto L. Burton, J. G. Cunningham, Comdr. Edward H. Cushing, Morris Fishbein, Don Hogate, O. J. Johnson, R. G. Leland, Major Sam F. Seeley, James Sterner and James T. Townsend.

To aid the medical profession in extending and improving its contribution to industrial medical service, medical societies in states and counties have been supplied with a program which will accelerate preparation. Medical and professional schools also have improved and expanded training programs. At present a joint report prepared by the Council on Industrial Health and the American Association of Industrial Physicians and Surgeons on improved industrial health education is in final stages of revision preceding publication and wide distribution to medical educators and organizations.

If industry is to absorb the products of accelerated industrial health education, some concomitant program of training industry in the advantages of medical supervision over workers is indispensable. The principal problem relates to small plants which are, or consider themselves, unable individually to support medical and nursing programs.

The Division of Industrial Hygiene of the U. S. Public Health Service reported that greater effort will be necessary to establish cooperation between bureaus of industrial hygiene and committees on industrial health in the various states. The annual budget for industrial hygiene in the U. S. Public Health Service amounts to about $650,000. Of the one hundred and sixty-one employees in the division, twenty-four are physicians and twenty-three are engineers. Medical and engineering studies have been conducted in government owned ordnance plants, quartermaster corps depots and air corps plants. Recommendations are being put into effect. Fifty-five government owned privately operated ordnance plants are certified for similar study. A reliable test for night vision is being sought, useful in the selection of pilots, truck drivers and night workers under blackout conditions. Other studies are to help in the selection of airplane pilots and bombardiers. Thirty-six states, four cities, two counties and two territories conduct industrial hygiene bureaus requiring a budget of $1,000,000 for 1942. During the year ended June 30, 1941, 6,084 investigations were made involving 1,509,797 workers. These bu eaus cooperate with the National Committee for the Conservation of Man Power in Industry and attempt to investigate plants having Walsh-Healy contracts. These state bureaus also supply consulting service in relation to dermatoses, nursing and sick absenteeism reporting. Over 90 per cent of the work of the research section of the Division of Industrial Hygiene deals with toxicity of explosives, solvents, chemicals and metals, the development of instruments for detection and measurement of exposures, high altitude effects, fatigue, and crowded working and living conditions. Miscellaneous activities include the preparation of a bibliography on mental hygiene in industry, inspection of plant medical services, development of educational pamphlets, radio scripts and films, preparation of technical standards in cooperation with the American Standards Association and advancement of plans for industrial nursing services, mainly of a part time character, to small industrial establishments.

Since adequate personnel is basic to a solution of medical service in industry, the Procurement and Assignment Service is charged with the avoidance of raiding industry of essential physicians and will do so if sufficient numbers of eligible medical people are available to fill military requirements. A reserve officer must immediately make a definite determination whether he is essential for industry or not and submit necessary representations to the adjutant general's office to obtain temporary deferment. Other physicians under 45 who are physically fit must be certified as absolutely essential to industry by the managements which hire them. Physicians in the 45 to 60 groups will be dislocated if certain specialist classifications are called up. In the over 60 group, dislocation is considered unlikely.

As substitutes for eligible and replaceable industrial physicians, reliance should be directed to physically unfit male physicians under 45, male physicians over 45, women physicians and, where possible, qualified laboratory and technical personnel whose employment in appropriate service would release an otherwise essential physician. Everything depends on the willingness of physicians on self analysis supplemented by advice from referees in counties, districts, states and corps areas to determine the physician's own greatest sphere of usefulness. Instructions will soon be issued enabling each physician to aline himself with service most consistent with his individual ability and physical equipment. Every physician will receive a certified serial number of his enrolment and an identifying button that only he will be authorized to wear.

Commissions on inactive status are under consideration in the U. S. Public Health Service, to be assigned to needed public health officers, physicians and sanitary engineers in order to have available means for coping with disaster and epidemics.

In order to acquaint the small manufacturers with the benefits of industrial health, it was agreed that some agency for public information be created. It was suggested that failure in this regard might logically lead to compulsory forms of industrial medical service. Specific suggestions included a presidential proclamation, followed by a broad but intensive campaign through newspaper and magazine articles, and organized promotion through local manufacturers' associations, chambers of commerce, civic organizations, medical publicity bureaus and every other accessible avenue. To implement these suggestions it was variously recommended:

(*a*) That a small conference be called soon in Washington to canvass the possibilities for better coordination in industrial health programs having particular reference to current plans in the Office for Civilian Defense and for creating an agency for public information.

(*b*) That the facilities of the Federal Security Agency be used to gain the same end.

(*c*) That the Subcommittee on Industrial Health and Medicine be enabled to employ necessary publicity talent.

(*d*) That the practicing physician can and must be relied on to provide medical service for small industry and that all programs of publicity and activities both in industrial hygiene and in civilian defense should bear this fact strongly in mind.

Although no precise action was taken, it seemed to be the general opinion that the chairman of the subcommittee inquire further into possibilities and that, if it seemed in the interests of the worker and industry, an agency for the dissemination of industrial health information be created. It seemed also to be the consensus that, if created, this agency should be directly attached to the subcommittee.

MEDICAL LEGISLATION

DISTRICT OF COLUMBIA

Bill Introduced.—S. 2394, introduced by Senator Bilbo, Mississippi, provides that the Commissioners of the District of Columbia shall cause to be set up facilities and shall appoint such personnel as they may deem necessary for the scientific determination of the degree of intoxication of motor vehicle drivers. The bill also provides for the admission in evidence of the results of the tests.

MEDICAL BILLS IN CONGRESS

Changes in Status.—H. R. 6730 has passed the House, a bill to protect the public health by regulating the mail order business in dentures. A companion bill, S. 2371, introduced by Senator Tunnell, Delaware, is pending in the Senate Committee on Interstate Commerce.

Bills Introduced.—S. J. Res. 140, introduced by Senator Glass, Virginia, proposes to grant permission to Hugh S. Cumming, Surgeon General (retired) of the United States Public Health Service, to accept certain decorations bestowed on him by the republics of Colombia, Haiti and Chile. S. 2405, introduced by Senator George, Georgia, proposes to discharge more effectively the obligations of the United States under certain treaties relating to the manufacture and distribution of narcotic drugs, by providing, through a licensure system, for domestic control of the production and distribution of the opium poppy and its products. S. 2412, introduced by Senator Pepper, Florida, proposes to provide benefits, including medical care, for the injury, disability, death or enemy detention of civilians and for the prevention and relief of civilian distress arising out of the present war.

STATE MEDICAL LEGISLATION

Virginia

Bill Introduced.—S. 141 proposes, among other things, to authorize the state hospital board to establish and maintain outpatient mental hygiene clinics, to establish and maintain mental health programs and services, and to initiate and direct the development of long range programs and plans with respect to mental hygiene and hospital services provided by the state.

Bill Passed.—S. 178, to amend the insurance law, proposes to authorize corporations issuing motor vehicle liability insurance to add endorsements thereto for the issuance of medical, surgical, ambulance or hospital payments to the insured.

Bill Enacted.—H. 171 authorizes the boards of supervisors of certain counties in the state to establish a retirement system for the employees of such counties and to employ such actuarial, medical and legal aid and assistance in establishing and administering such system as it may deem necessary.

WOMAN'S AUXILIARY

WINNERS IN THE HYGEIA CONTEST

The American Medical Association offered $400 in cash prizes to the state and county auxiliaries which obtained the largest number of subscription credits to *Hygeia*. The contest covered the period from Sept. 1, 1941 to Jan. 31, 1942.

Cash prizes were awarded as follows:

Group 1. Auxiliaries with a membership of from one to thirteen:

First prize, $40, to Perry County, Mo., Mrs. B. T. Koon, president, Perryville, Mo.

Second prize, $25, to Cass County, Mo., Mrs. David S. Long, Hygeia chairman, Harrisonville, Mo.

Third prize, $15, to Childress-Collingsworth-Hall counties, Texas, Mrs. J. A. Odom, Hygeia chairman, Memphis, Texas.

Group 2. Auxiliaries with a membership of from fourteen to twenty-three:

First prize, $40, to Chelan County, Wash., Mrs. R. S. Mitchell, Hygeia chairman, Wenatchee, Wash.

Second prize, $25, to Cowlitz County, Wash., Mrs. C. J. Sells, Hygeia chairman, Longview, Wash.

Third prize, $15, to Twin Falls County, Idaho, Mrs. C. B. Beymer, Hygeia chairman, Twin Falls, Idaho.

Group 3. Auxiliaries with a membership of from twenty-four to forty-two:

First prize, $40, to Walla Walla Valley, Wash., Mrs. J. T. Rooks, Hygeia chairman, Walla Walla, Wash.

Second prize, $25, to Bowie-Miller counties, Texas-Ark., Mrs. Ralph Cross, Hygeia chairman, Texarkana, Texas.

Third prize, $15, to Vermilion County, Ill., Mrs. C. L. Bennett, Hygeia chairman, Danville, Ill.

Group 4. Auxiliaries with a membership of from forty-three to six hundred:

First prize, $40, to Westmoreland County, Pa., Mrs. I. J. Ober, Hygeia chairman, Greensburg, Pa.

Second prize, $25, to Buchanan County, Mo., Mrs. Charles H. Werner, Hygeia chairman, St. Joseph, Mo.

Third prize, $15, to Cook County, Ill., Mrs. Clyde R. Landis, Hygeia chairman, Chicago.

State winners:

First prize, $40, to state of Washington, Mrs. Delmar F. Bice, Hygeia chairman, Yakima, Wash.

Second prize, $25, to state of Illinois, Mrs. E. M. Egan, Hygeia chairman, Chicago.

For the third prize, $15, no state qualified by sending in their quota of subscriptions.

Honorable Mention was given to the following counties:

Santa Barbara County, Calif., Mrs. H. E. Henderson, chairman, Santa Barbara.

Arapahoe County, Colo., Mrs. H. B. Catron, chairman, Englewood.

Richmond County, Ga., Mrs. E. S. Sanderson, chairman, Augusta.

Bannock-Bingham County, Idaho, Mrs. W. W. Beck, chairman, Blackfoot.

Rock Island County, Ill., Mrs. Samuel Brown, chairman, East Moline.

Wayne County, Mich., Mrs. F. T. McCormick, chairman, Detroit.

Muskogee County, Okla., Mrs. J. T. Woodburn, Muskogee.

Mercer County, Pa., Mrs. Paul T. Hope, chairman, Mercer.

Spartanburg County, S. C., Mrs. W. T. Hendrix, chairman, Spartanburg.

Snohomish County, Wash., Mrs. Lewis J. Ferrell, chairman, Everett.

Raleigh County, W. Va., Mrs. A. C. Echols, chairman, Prince.

Brown-Kewaunee-Door counties, Wis., Mrs. L. D. Quigley, chairman, Green Bay.

Other counties that have reached or exceeded their quota were Kern County, Calif.; Monterey-San Benito County, Calif.; Riverside County, Calif.; Duval County, Fla.; Sangamon County, Ill.; Dubuque County, Iowa; Shawnee County, Kan.; Renville County, Minn.; Greene County, Mo.; Jackson County, Mo.; Montgomery County, N. Y.; Pottawatomie County, Okla.; Marion-Polk County, Ore.; Berks County, Pa.; Bucks County, Pa.; Crawford County, Pa.; Mifflin County, Pa.; Clark County, Wash.; King County, Wash.; Pierce County, Wash.; Whatcom County, Wash.; Yakima County, Wash.; Kenosha County, Wis.; Racine County, Wis.; Rock County, Wis.

This year's contest resulted in eight thousand one hundred and seventy-four subscriptions.

To the Hygeia chairmen, officers and members of the various county and state woman's auxiliaries who have assisted in making this contest a success, Mrs. George R. Dillinger, national Hygeia chairman, and the circulation manager of *Hygeia* express appreciation.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

New Health Officer for Birmingham.—Dr. George A. Denison, acting health officer of Birmingham and Jefferson County since September, has been appointed health officer, effective February 25. Dr. Denison graduated at Baylor University College of Medicine, Dallas, Texas. He has been connected with the Jefferson County health unit since 1921. From 1931 until his appointment as acting health officer he served as director of the bureau of laboratories.

State Medical Meeting in Montgomery.—The annual session of the Medical Association of the State of Alabama will be held at the Whitley Hotel, Montgomery, April 21-23, under the presidency of Dr. James M. Mason, Birmingham, and with the Montgomery County Medical Society acting as host. Included among the speakers will be:

Dr. Ralph McBurney, Tuscaloosa, A Clinical Evaluation of the Erythrocyte Sedimentation Rate.
Dr. Henry B. Burdeshaw, Dothan, Blood and Blood Substitutes in the Treatment of Hemorrhage and Shock.
Drs. Frank A. Kay, James D. Smith and Norman H. Reim, Tuscaloosa, Electric Shock Treatment in Psychiatric Disorders.
Dr. French H. Craddock Jr., Sylacauga, Intravenous Alcohol in Postoperative Analgesia.
Dr. Ralph M. Clements, Tuscaloosa, A Newer Treatment for Perennial Hay Fever.

One general session will be addressed by out of state physicians, Drs. Edward L. Compere, Chicago, speaking on "The Treatment of Compound Fractures" and Frank E. Adair, New York, "Carcinoma of the Breast." Part of another general session will be devoted to a panel discussion on poliomyelitis by Drs. Daniel G. Gill, Montgomery, epidemiology; Albert E. Casey, New Orleans, pathology; Carl A. Grote, Huntsville, the acute state, and H. Earle Conwell, Birmingham, muscular rehabilitation. Dr. Harvey B. Stone, Baltimore, will deliver the Jerome Cochran Lecture Wednesday morning on "Biliary Diseases as Seen by the Surgeon."

CONNECTICUT

Section for Industrial Physicians.—With the February issue, *Connecticut Industry*, official organ of the Manufacturers Association of Connecticut, will conduct a regular column to promote an exchange of ideas among industrial physicians to help further the adoption of improved industrial medical procedures in Connecticut industries.

Grant for Research on Child Development.—The Carnegie Corporation of New York has given a grant of $10,000 to support a research program at the Clinic of Child Development at Yale University School of Medicine, New Haven. The clinic, which was founded in 1911 by Dr. Arnold L. Gesell, its present director, is investigating the mental growth of normal infants and devising clinical methods for the early diagnosis of developmental defects and deviations. Staffed by pediatricians and psychologists, it maintains a diagnostic and advisory service for infants and preschool children, a guidance nursery, a photographic research library and special facilities for one way vision observation and for systemic studies of normal and abnormal child behavior.

DISTRICT OF COLUMBIA

Biochemist Receives Hillebrand Award.—Michael X. Sullivan, Ph.D., since 1931 director of the Chemo-Medical Research Institute, Georgetown University School of Medicine, Washington, was presented with the Hillebrand Award of the Chemical Society of Washington at the annual dinner, March 12, for his work on the "Sulfur-Containing Substances of the Body." Dr. Sullivan received his Ph.D. at Brown University, Providence, R. I., in 1903. He served as fertility expert at the Bureau of Soils, U. S. Department of Agriculture, from 1907 to 1915 and as biochemist to the U. S. Public Health Service from 1915 to 1931. He was president of the Washington Section of the American Chemical Society in 1914.

Hospital Meeting.—The fifth annual meeting of the Medical Society of St. Elizabeths Hospital, Washington, will be addressed, April 18, by Dr. Lucille Dooley, Washington, on "Psychoanalytical Concepts of Manic Depressive Psychosis"; Nathan Bryliion Fagin, Ph.D., Baltimore, "The Influence of Psychoanalysis on Modern Literature"; Dr. Uno H. Helgesson, Commander, U. S. Naval Reserve, Washington, "Acute Traumatic Neuroses Following Combat," and Dr. Winfred Overholser Washington. Elmer Louis Kayser, Ph.D., Washington, will be the speaker at the annual dinner.

FLORIDA

State Medical Meeting in Hollywood April 13-15.—The sixty-ninth annual meeting of the Florida Medical Association will be held at the Hollywood Beach Hotel, Hollywood, April 13-15, under the presidency of Dr. Walter C. Jones Jr., Miami. The Palm Beach County Medical Society will be host at the session. Included among the speakers will be:

Dr. Lauren M. Sompayrac, Lieutenant, U. S. Navy, Naval Hospital, Jacksonville, The Dermatologist in the Navy.
Dr. James A. Bradley, St. Petersburg, Bed Rest in Coronary Thrombosis.
Dr. Nathan S. Rubin, Major, U. S. Army, Station Hospital, Panama City, Some Medical Problems of Flight.
Dr. Daniel C. Elkin, Atlanta, Ga., Injuries of the Chest.
Dr. Harold G. Nix, Tampa, Use of Vitamin K in Obstetrics.
Drs. Wilfred McL. Shaw and William Tracy Haverfield, Jacksonville, Roentgen Aids in the Diagnosis and Localization of Intracranial Conditions.
Dr. Warren W. Quillian, Coral Gables, Pyurias in Childhood: Their Significance and Treatment.

Other groups meeting at this time include the Florida section of the American College of Physicians, the Florida Radiological Society, the Florida Pediatric Society and the Florida Association of Dermatology and Syphilology. Dr. Cornelius F. Holton, Savannah, Ga., will discuss "Industrial Surgery" before the Florida Association of Industrial Surgeons, and Dr. Frank E. Burch, St. Paul, "Cataracts" and "Glaucoma" before the Florida Society of Ophthalmology and Otolaryngology. The sixteenth annual meeting of the woman's auxiliary to the state medical association will be held, April 13-15.

ILLINOIS

Change in Hospital Superintendents.—Dr. Joseph H. Ellingsworth, Geneseo, has been appointed managing officer of the Peoria State Hospital, succeeding Dr. Philip Waters, who has assumed a similar position at the East Moline State Hospital. Dr. Waters fills the vacancy that occurred when Dr. Joseph A. Campbell resigned.

Coordinators Named to Protect Water Supply.—A group of coordinators from ten emergency water corps zones has been appointed to work toward the protection and conservation of existing water supply systems in more than six hundred down state municipalities. A meeting was held in Springfield, March 12, under the auspices of the state department of health to map out regulations and programs for local application.

Chicago

Society News.—Dr. Frederic Schreiber, Detroit, discussed "Clinical Relationship Between Cerebral Anoxia and Anesthesia" before the Chicago Society of Anesthetists, February 25.——The Chicago Laryngological and Otological Society was addressed, March 2, by Drs. John H. Gilmore on "X-Ray Studies in Mastoid Pathology"; Oliver McGillicuddy, Lansing, Mich., "Encephalomeningoceles in the Nasal Cavities," and Mauritius Tamari, "Histopathologic Changes of the Temporal Bone in Paget's Disease."——The Illinois Psychiatric Society, March 5, was addressed by Drs. Milton Rosenbaum, Cincinnati, "Adaptation of the Central Nervous System to Alcohol"; James Clark Moloney, Detroit, "Unconscious Motivations for the Choice of Employment," and Maxwell Gitelson, "The Critical Moment in Psychotherapy."——The North Shore Branch of the Chicago Medical Society will be addressed at the Sovereign Hotel, April 7, by Dr. Bayard T. Horton, Rochester, Minn., on "Headaches: Clinical Types and Treatment." The North Side Branch was addressed, March 5, by Drs. Ernest H. Falconer, San Francisco, on "Hodgkin's Disease, with Special Reference to Skeletal and Bone Marrow Involvement" and Edward L. Bortz, Philadelphia, "Geriatrics: A New Light on Old Folks."

LOUISIANA

State Medical Meeting.—The Louisiana State Medical Society will hold its annual meeting in New Orleans, April 27-29, under the presidency of Dr. Paul King Rand, Alexandria. Among the out of state speakers will be Drs. Jacob Arnold Bargen, Rochester, Minn., on "The Use of Sulfonamide Derivatives in the Digestive Tract"; Charles T. Stone, Galveston, Texas, "The Future of the Coronary Thrombosis Patient"; Adolph B. Loveman, Louisville, "Some Cutaneous Manifestations of Systemic Disorders," and Roy F. Baskett, Texarkana,

Ark., "The Use of the Various Insulins in the Treatment of Diabetes Mellitus." The program will include the following local physicians:

Dr. Frank L. Loria, New Orleans, Abdominothoracic Gunshot Injuries.
Drs. Bjarne Pearson and Manuel M. Garcia, New Orleans, Spread and Metastasis in Carcinoma of the Cervix Uteri.
Drs. Daniel N. Silverman, Robert A. Katz and Andrew V. Friedrichs, New Orleans, The Increasing Incidence and Complications of Chronic Bacillary Dysentery.
Dr. Charles R. Gowen, Shreveport, The Rational Management of Bronchiectasis.
Drs. Louis S. Charbonnet Jr. and George F. Schroeder, New Orleans, The Physiologic Conception of Tissue Resistance in the Surgical Diabetic.

One session will be devoted to a symposium on "Health Protection of Civilians in the Present War" to cover the subjects of nutrition, emergency water supply and sewage disposal, potential epidemics in Louisiana, protection by immunization and provisions for children.

MICHIGAN

New Director of Epidemiology.—Dr. Thaddeus M. Koppa, assistant director of epidemiology, Michigan State Department of Health, Lansing, has been appointed director, newspapers report. He succeeds Dr. Wallace M. Chapman, who has resigned to enter private practice in California. Dr. Chapman was named to the position last year.

Health Center Opened.—The new Delta County Health Center at Escanaba was opened formally to the public on February 8. The center is in a former school building, which was remodeled to meet the needs for offices of the county school commissioner and for the health unit of the county. There are six rooms, a library and a meeting room with a seating capacity of between seventy-five to one hundred persons. Dr. Fred O. Tonney, Escanaba, is director of the county health unit.

MINNESOTA

Meeting of Radiologists.—The spring meeting of the Minnesota Radiological Society was held at the Mayo Foundation House, Rochester, March 28. The speakers included the following Rochester physicians:

Drs. William C. MacCarty Jr. and Byrl R. Kirklin, Radiologic and Pathologic Studies of Prepyloric Ulcer.
Drs. Frank J. Rigos, Oak Terrace, and John D. Camp, Primary Tumors of the Ribs.
Drs. James T. Shelden and Walter C. Popp, X-Ray Treatment of Erysipelas.
Drs. Robert D. Moreton and Eugene T. Leddy, Dysgerminomas with Reference to Radiosensitivity.
Drs. George R. Dochat and Malcolm B. Dockerty, Prognosis in Carcinoma of the Stomach in Relationship to Duke's Type and Broder's Grade of Malignancy.

At the evening session Dr. Patrick P. T. Wu, Tsang, Peiping, China, gave an address entitled "China Speaks."

MISSOURI

State Meeting in Kansas City April 27-29.—The annual session of the Missouri State Medical Association will be held in the Municipal Auditorium, Kansas City, April 27-29, under the presidency of Dr. Robert B. Denny, Creve Coeur. Out of state speakers will include:

Dr. Karl W. Brimmer, Washington, D. C., Faith, Hope and Cure-Alls.
Dr. Waltman Walters, Rochester, Minn., Gastric Ulcer.
Dr. Willard R. Cooke, Galveston, Texas, Three Important Advances in Obstetric Therapy: Analgesia, Intravenous Ergotrate in Third State of Labor, Magnesium Sulfate in Eclampsia.
Dr. George R. Herrmann, Galveston, Some Medical Emergencies and Their Management.
Dr. Russell L. Haden, Cleveland, The Differentiation of Obscure Anemia.
Dr. Cobb Pilcher, Nashville, Tenn., Neurosurgery in the War.
Dr. Joe Vincent Meigs, Boston, Endometriosis.
Dr. Arthur Purdy Stout, New York, Clinical Diagnosis of Cancer of the Breast.
Dr. Robert Elman, St. Louis, The Correction of Acute Protein Deficiency in the Treatment of Surgical Shock, Severe Hemorrhage and Burns.
Dr. Hobart A. Reimann, Philadelphia, Practical Aspects of Newly Discovered Forms of Pneumonia.
Dr. Harris B. Shumacker Jr., Baltimore, The Value of Sympathectomy in the Treatment of Peripheral Vascular Disorders.
Dr. Irvine H. Page, Indianapolis, Hypertension and Its Experimental Treatment.
Dr. Raymond O. Muether, St. Louis, Blood Banks.
Dr. Oliver Cope, Boston, Hyperthyroidism.
Dr. William B. Kountz, St. Louis, The Recognition and Treatment of Degenerative Health Disease.
Donald E. Cummings, B.S., Denver, Industrial Health.

The annual banquet, Monday evening, will be addressed by Dr. George F. Lull, colonel, M. C., U. S. Army, Washington, D. C., on "The Medical Officer in Our Wartime Army." Dr. Willard R. Cooke will also address the maternal welfare luncheon meeting.

NEW HAMPSHIRE

Changes in Board of Health.—Dr. Ralph E. Miller, associate professor of pathology and assistant dean of Dartmouth Medical College, Hanover, has been chosen president of the state board of health to succeed Dr. George C. Wilkins, Manchester, who retired after serving in this capacity for many years. The latter had been a member since 1915. Dr. Montfort Haslam, Antrim, has been named a member of the board, succeeding Dr. James W. Jameson, Concord, a member since 1933, who also retired.

NEW JERSEY

Health Officers Association.—Mr. W. Stanley Applegate, Asbury Park, was elected president of the New Jersey Health Officers' Association, succeeding Mr. Harold W. Hager, Ocean City; Mr. Hugh B. Martin, Englewood, was elected vice president and Mr. William C. Blake, Princeton, reelected secretary-treasurer.

NEW YORK

Public Sunday Medical Lectures.—As a public service and a contribution to the war effort, the University of Buffalo School of Medicine, Buffalo, recently conducted a series of five public lectures on "The Care of Your Health During the War." The lectures, which were given in the amphitheater of the medical school, started on February 8. The medical school gave a course of public lectures last year also as a community service.

Fifty Years as Health Officer.—Dr. Morris W. Cowden, Gerry, Chautauqua County, was recently presented with a testimonial letter by Dr. Edward S. Godfrey Jr., state health commissioner, "in recognition of fifty years of faithful and continuous service as health officer." Dr. Cowden graduated at the University of Buffalo School of Medicine in 1890. He had been practicing in Gerry for two years when he was named health officer. Dr. Cowden has retired from active practice but still carries on as local health officer.

Maternal and Child Welfare Teaching Day.—A group of local agencies sponsored a regional maternal and child welfare teaching day at the Rochester General Hospital, Rochester, April 1. Included among the speakers were:

Drs. Donald H. Kariher and Howard A. Spindler, Rochester, The Role of the Blood Rh Factor in Transfusion Reactions and Erythroblastosis Fetalis.
Dr. John M. MacMillan, Rochester, Tuberculosis and Pregnancy.
Dr. Herbert C. Soule, Rochester, The Care of the Premature Infant.
Dr. Charles S. Lakeman, Rochester, The Diagnosis and Treatment of Thrombophlebitis.
Dr. Clarence Arthur Elden, Rochester, The Treatment of Habitual Abortion.
Dr. Ferdinand J. Schoeneck, Syracuse, Demonstration of Case Study.

Dr. Harvey B. Matthews, Brooklyn, clinical professor of obstetrics and gynecology, Long Island College of Medicine, addressed the evening session at the Rochester Academy of Medicine on "Prolonged Labor: Etiology and Management."

New York City

The Janeway Lectures.—The annual Edward Gamaliel Janeway Lectures at Mount Sinai Hospital will be delivered by Michael Heidelberger, Ph.D., associate professor of biochemistry, Columbia University College of Physicians and Surgeons, April 7 and April 10. His subject will be "Newer Concepts of Infection and Immunity and Chemistry's Part in Their Development."

Physician Wins Town Hall Essay Contest.—Dr. Jacob Sobel, attending pediatrician at the Hospital for Joint Diseases and Beth David Hospital and director of pediatrics at Gouverneur Hospital, recently won first prize of $250 in the national essay contest sponsored by Town Hall in connection with its radio forum, America's Town Meeting of the Air. The subject was "What Must We Do to Improve the Health and Well-Being of the American People?" Dr. Sobel graduated at Columbia University College of Physicians and Surgeons in 1895.

Dr. Bernecker New Commissioner of Hospitals.—Dr. Edward M. Bernecker, general medical superintendent for the city department of hospitals, has been named commissioner of hospitals to succeed Dr. Willard C. Rappleye, resigned. Born in Seward, Neb., March 13, 1892, Dr. Bernecker graduated at the Hahnemann Medical College and Hospital in Chicago in 1915. He served his internship at Metropolitan Hospital. In 1917 he entered the U. S. Army and was appointed a surgeon in the air service. According to the New York *Times* he was stationed in the second A. E. F. training section at Tours in France and later was appointed a battalion surgeon in the second division. After the war he returned to Metropolitan

Hospital as deputy superintendent, becoming superintendent in 1930. In 1935 he became deputy superintendent of the Kings County Hospital, leaving the position in 1937 to become general medical superintendent for the department of hospitals.

Professional Service Building Dedicated.—The Hospital for Joint Diseases February 7 dedicated its new professional service building, the Melanie Faith Polachek Cournand Memorial. The building is seven stories high and contains professional facilities and services to serve both outpatients and inpatients. The first floor contains emergency room, admitting offices for ward patients, medical emergency field unit and the central offices of the social service department. The physical therapy department is on the second floor and the radiology service on the third. The Women's Division, including facilities for about two hundred and fifty women volunteers, sewing rooms for hospital linens, patients' circulating library and reading room and the occupational therapy department, is on the fourth floor. The fifth floor contains a blood bank, bacteriology laboratory and an auditorium; the sixth, laboratories for surgical pathology, clinical pathology and research; the seventh, animal operating rooms. The various units were financed by individual donors.

Physicians Honored by Polyclinic Hospital.—Exercises were held at the Polyclinic Medical School and Hospital, February 10, to honor twenty-three physicians and surgeons "deemed to have contributed most toward the creation" of the hospital. Portraits of the physicians were unveiled. Dr. Orrin S. Wightman, formerly president of the state medical society, presented the portraits to the hospital and Dr. Joseph F. McCarthy, president of the faculty, accepted the gift, which is said to represent graphic portrayal of the sixty-one year history of Polyclinic Hospital. The complete list of those whose portraits appear in the gallery follows: Drs. Willard Parker, Paul F. Munde, Andrew R. Robinson, Landon Carter Gray, Abraham Jacobi, Walter Gill Wylie, Arpad G. Gerster, Virgil P. Gibney, D. Bryson Delavan, Luther Emmett Holt, Bernard Sachs, James P. Tuttle, James Riddle Goffe, William Rice Pryor, Robert C. Myles, Frederick Whiting, Charles Gilmore Kerley, John A. Bodine, Royal Whitman, Orrin S. Wightman, Frederick H. Dillingham, John Allen Wyeth and Harry Marion Sims. With the exception of seven men, Drs. Delavan, Sachs, Whiting, Kerley, Whitman, Wightman and Dillingham, the honored men are dead.

OHIO

Regional Meeting on Anesthesia.—The American Society of Anesthetists, Inc., the Ohio State Section of the national society and the Ohio Society of Anesthetists will meet at the Neil House, Columbus, April 30, for the following program:

Dr. Norris E. Lenahan, Columbus, Intravenous Anesthesia.
Dr. Harold D. Green, Cleveland, Shock.
Dr. James H. Bennett, Cincinnati, The Anesthetic Management for Drainage of Abscess of the Submandibular Space.
Dr. Kenneth C. McCarthy, Toledo, Casualty Anesthesia in England.
Drs. John K. Potter and Reynold M. Crane, East Cleveland, Anesthesia in Thyroid Surgery.
Dr. Abe L. Schwartz, Cincinnati, The Use of Picrotoxin in Barbiturate Poisoning.

New Professor of Dermatology and Syphilology.—Dr. Harry L. Claassen, assistant professor of dermatology and syphilology at the University of Cincinnati College of Medicine, has been promoted to professor, effective March 3. He fills the vacancy caused by the death of Dr. Elmore B. Tauber, Jan. 23, 1941. Dr. Claassen has been assistant professor and acting head of the department. With his promotion Dr. Claassen also became director of the service of dermatology and syphilology in the Cincinnati General Hospital. He graduated at Cincinnati in 1918 and has been a member of the staff since 1922.

Annual Postgraduate Day.—The Mahoning County Medical Society will observe its annual postgraduate day at the Pick-Ohio Hotel, Youngstown, April 15, with the following program:

Dr. Jacob R. Buchbinder, Acute Diffuse Peritonitis: Pitfalls in Diagnosis and Some More Recent Concepts of Treatment; Present Status of Surgery for Duodenal Ulcer.
Dr. Harry Culver, Traumatic Conditions of the Male Urethra and Bladder; Nonspecific Upper Urinary Tract Infections.
Dr. Paul S. Rhoads, Clinical Feature and Treatment of Pneumonia, 1941-1942 Season; Hemolytic Streptococcus Infections of the Throat and Nose: Their Importance as a Clinical and Public Health Problem.
Dr. George H. Gardner, Pelvic Endometriosis—An Increasingly Frequent Clinical Problem; Management of the Barren Marriage.

All the speakers are members of the faculty of Northwestern University Medical School, Chicago.

OREGON

Annual Meeting of Surgeons.—The annual session of the Spokane Surgical Society will be held at the Davenport Hotel, Spokane, April 25, with Dr. Richard B. Cattell, Boston, as the guest speaker. The titles of Dr. Cattell's lectures will be "Diseases of the Thyroid Gland," "Common Duct Obstructions" and "Selection of Operation for Carcinoma of Colon and Rectum."

WISCONSIN

New Tuberculosis Officers.—Dr. George C. Owen, Oshkosh, was recently elected president of the Wisconsin Trudeau Society; Dr. Einar R. Daniels, Milwaukee, vice president, and Dr. John D. Steele Jr., Milwaukee, secretary.

Dearholt Fund to be Continued.—The Dearholt Memorial Fund, established by the late Dr. Hoyt E. Dearholt, Milwaukee, former executive secretary of the Wisconsin Anti-Tuberculosis Association, will be maintained permanently, it has been announced. Tuberculosis institutes at Marquette University School of Medicine, Milwaukee, and the University of Wisconsin Medical School, Madison, as well as at sanatoriums throughout the state, are made possible by the fund. Dr. Dearholt started the fund by making deductions from his salary as secretary of the association.

Physician Honored.—More than a hundred former patients of Dr. George V. I. Brown gave a dinner in his honor in Milwaukee, February 15. Dr. Brown, who is 80 years of age, recently retired from active practice and is doing consultation work only. He was professor of oral and plastic surgery at the University of Wisconsin Medical School, Madison, from 1920 until he retired as emeritus professor in 1937. During World War I he was called to the Office of the Surgeon General, Washington, as chief of the plastic and oral service at Walter Reed Hospital. Under the orders of General Gorgas he established a school for training men in plastic surgery at Fort Oglethorpe, Ga., before they went overseas.

GENERAL

Blood Plasma Package Wins Award.—Sharp and Dohme, Inc., was given the top award in the drugs, chemicals and drug sundries classification of the eleventh annual All-America Package Competition sponsored by *Modern Packaging* Magazine recently for a package developed to supply dehydrated human blood in a portable, practical and stable form for use in war and civilian practice. The package is supplied as a complete unit with the exception of the intravenous outfit, which is supplied in a separate package and is always included with each order unless otherwise specified.

Grants for Research.—William R. Warner & Company, Inc., New York, has announced grants for medical research as follows:

The Long Island College of Medicine, Brooklyn, a two year fellowship for postgraduate study in the department of radiology.

New York University College of Medicine, New York, for the study of the conjugation of the sulfonamide drugs. This study will be carried out in the pneumonia service of the Harlem Hospital.

Northwestern University Medical School, Chicago, for the study of toxic factors as observed in the department of dermatology investigating the possibilities of detoxifying therapeutic agents used in the practice of dermatology.

Washingtonian Hospital, Boston, for the study of alcoholism involving the blood chemistry and psychometric findings of cases while under the influence of alcohol and during recovery.

Changes in Status of Licensure.—The California State Board of Medical Examiners reports the following:

Dr. Howard D. Mayers, Fall River Mills, license revoked, Oct. 22, 1941, for habitual intemperance.

Dr. Frederick William Riley, Los Gatos, license revoked Oct. 23, 1941, charged with aiding and abetting an unlicensed individual, i. e. William F. Hoque, who operated the Valley Rest Home, Los Gatos, where patients were treated with an escharotic paste as an asserted "cure" of cancer.

Dr. Oscar Charles Long, Brawley, license restored October 21; he was placed on five years' probation without narcotic privileges and ordered to report at each Los Angeles meeting.

The Medical Grievance Committee of the New York State Education Department announces the following action:

Dr. Archie Max Fisher, Spencer, N. Y., license revoked in September 1941 for drug addiction.

Director of Planned Parenthood Federation Appointed.—Dr. Claude C. Pierce, until March 1 medical director of the U. S. Public Health Service in charge of district number 1, New York, has been appointed national medical director of the Planned Parenthood Federation of America, Inc., formerly known as the Birth Control Federation of America, Inc., according to an announcement from the society's headquarters in New York. Dr. Pierce graduated at Chattanooga Medical College in 1898. In 1900 he joined the public health service.

In 1918 an act passed by congress creating the United States Interdepartmental Social Hygiene Board became a law. This included the establishment of a division of venereal diseases in the U. S. Public Health Service. Dr. Pierce organized and directed this division as assistant surgeon general in charge for four years, serving also during that time as a member of the Interdepartmental Social Hygiene Board. When the newly created position of district director was established in 1922 he was assigned to Chicago in charge of district number 3. Later he went to Mexico and Cuba to confer with government authorities on sanitary conditions and quarantine restrictions. In 1926 he was assigned to Washington as assistant surgeon general in charge of personnel and accounts. Subsequently he went to Europe for supervision of medical inspection of aliens. In 1937 he was relieved of duty in Europe and assigned as director of public health district number 1 with headquarters in New York City.

Educational Program on Diabetes. — The Metropolitan Life Insurance Company has been conducting an educational program on diabetes during the past year. More than one and one-half million pamphlets were distributed to the public and to interested physicians. New publications for the public were printed. Exhibits, conferences and correspondence were used to interest health officers and health departments in diabetes control. About one hundred and ten meetings have been addressed by the company's examiners or other physicians. A number of state medical societies actively participated in the program. The objectives of this program are a wider recognition of incipient symptoms, the early detection of disease by medical examination and urinalysis, a closer working relationship between the potential or actual diabetic patient and the private medical practitioner, and more thorough and adequate treatment with postponement of mortality, together with more widespread information about the possible preventive factors.

American Pediatric Society. — The fifty-fourth annual meeting of the American Pediatric Society will be held at Skytop, Pa., April 30-May 2. There will be a symposium on children in the civilian defense program and one on the control of communicable diseases in defense areas and among civilian populations. Among the speakers will be:

Drs. Clement A. Smith and Eugene Kaplan, Boston, Adjustment of Blood Oxygen Levels in Neonatal Life.
Dr. Henry F. Helmholtz, Rochester, Minn., Experimental Studies in Treatment of Urinary Infections.
Dr. Lewis K. Sweet, Washington, D. C., Chemotherapy in Acute Gonococcal Conjunctivitis.
Drs. Luther Emmett Holt Jr. and Victor A. Najjar, Baltimore, A Simple Method for the Laboratory Diagnosis of Deficiencies of Thiamine, Riboflavin and Nicotinic Acid.
Dr. Harold L. Higgins, Boston, Some Physiologic Aspects of Acidosis.
Dr. Arthur F. Abt, Dr. L. Martin Hardy, Chester J. Farmer, A.M., and Jessie D. Maske, all of Chicago, Relation of Vitamin C to Scarlet Fever, Rheumatic Infections and Diphtheria in Children.
Drs. Harold K. Faber and Edward B. Towne, San Francisco, Surgical Treatment of Cranial Synostosis with Special Reference to Prevention of Blindness.
Dr. Bert I. Beverly, Chicago, Anxieties in Childhood.

Annual Meeting of College of Physicians.—The twenty-sixth annual session of the American College of Physicians will be held at the Municipal Auditorium in St. Paul, April 20-24, under the presidency of Dr. Roger I. Lee, Boston. "Medical Horizons" is the theme of the meeting. The program of the general sessions complements that of the clinics, panel discussions and morning lectures, which will be held throughout the week. Included among the speakers of the six general sessions will be:

Drs. Edgar V. Allen and Nelson W. Barker, Rochester, Minn., Clinical Studies on the Prevention of Venous Thrombosis and Pulmonary Embolism by the Use of a Preparation from Spoiled Sweet Clover Which Prolongs Coagulation and Prothrombin Time of the Blood.
Dr. Oswald F. Hedley, Bethesda, Md., U. S. Public Health Service, The Fraudulent Use of Digitalis to Simulate Heart Disease.
Dr. Walter S. McClellan, Saratoga Springs, N. Y., New Trends in Treatment of Chronic Disease; An Experience in Spa Therapy.
Dr. Martin Henry Dawson, New York, Penicillin as a Chemotherapeutic Agent.
Dr. Chester S. Keefer, Boston, Gramicidin in the Treatment of Local Infections.
Dr. Nathan S. Davis III, Chicago, Factors Which May Influence Senescence.

A symposium on aviation medicine will constitute the afternoon's program at the first general session Monday with the following speakers: Drs. Louis H. Bauer, Hempstead, N. Y., on "A Brief History of Aviation Medicine and the Physical Qualifications for Flying"; John R. Poppen, captain, M. C., U. S. Navy, Washington, D. C., "Effects of High Speed Including Dive Bombing; Aero Embolism," and Harry G. Armstrong, M. C., U. S. Army, Randolph Field, Texas, "Want and the Use of Supplementary Oxygen." On Wednesday afternoon another general session will be devoted to communicable diseases. At the annual convocation on Wednesday evening, Dr. Lee will deliver his presidential address and Dr. William deB. MacNider, Kenan research professor of pharmacology, University of North Carolina School of Medicine, Chapel Hill, N. C., will give the convocational address on "A Consideration of the Factor of Change in the Animal Organism." The John Phillips Memorial Medal for 1941-1942 will be presented at this meeting.

The Nutrition Foundation. — Sixteen food companies recently cooperated in creating the Nutrition Foundation, Inc., to develop and apply the science of nutrition for the improvement of the diet and health of the American people. Officers include George A. Sloan, New York City Commissioner of Commerce, president; Charles Glen King, Ph.D., professor of chemistry, University of Pittsburgh, vice president; Ole Salthe, formerly director of the Bureau of Food and Drugs, Department of Health, New York, and more recently consultant of the Food and Drug Administration, Federal Security Agency, Washington, D. C., executive secretary, and Karl T. Compton, Sc.D., Cambridge, Mass., president of the Massachusetts Institute of Technology, chairman of the board. The new group held its inaugural dinner on March 12 in New York. On March 16 the organization of a scientific advisory committee for the foundation was announced. Members are Dr. Frank G. Boudreau, executive director, Milbank Memorial Fund, New York; Conrad A. Elvehjem, Ph.D., University of Wisconsin, Madison; Icie M. Hoobler, Ph.D., Children's Fund of Michigan, Detroit; Paul E. Howe, Ph.D., Surgeon General's Office, U. S. Army, Washington, D. C.; Elmer V. McCollum, Ph.D., Johns Hopkins University School of Hygiene and Public Health, Baltimore; Leonard A. Maynard, Ph.D., Cornell University, Ithaca, N. Y.; John R. Murlin, Ph.D., University of Rochester, Rochester, N. Y.; Roy C. Newton, Ph.D., Swift & Co., Chicago; Lydia J. Roberts, Ph.D., Department of Home Economics, University of Chicago; William C. Rose, Ph.D., University of Illinois, Urbana, Ill.; Dr. William H. Sebrell Jr., U. S. Public Health Service, Washington, D. C.; Henry C. Sherman, Ph.D., Columbia University, New York; Dr. Frederick F. Tisdall, University of Toronto, Toronto, Canada, and Robert R. Williams, Sc.D., chemical director, Bell Telephone Laboratories, New York. There is also a food industries advisory committee. The sixteen founder companies of the new foundation have guaranteed $10,000 a year each for over a five year period, although it is hoped that eventually increased funds will be received to expand both research and service. Membership in the foundation of the corporation is to consist of three classes: founder members, sustaining members and public members. There shall be one annual meeting of the corporation.

LATIN AMERICA

Committee for Medical Defense.—The Medical Federation of Cuba recently formed a committee on medical defense with Dr. Pedro L. Farinas Mayo, Havana, Cuba, as director. A meeting was held January 23 by Drs. Moisés Chediak, Havana, on "National Organization of Departments for Blood Transfusion," and Guillermo López Rovirosa, Havana, on "Importance of Establishing Laws for Food Rations in Any Possible Difficulties."

Deaths in Other Countries

Sir Henry Britten Brackenbury, chairman of the council of the British Medical Association; from 1915 to 1924 chairman of the Insurance Acts Committee and until 1927 chairman of its representative body; member of the General Medical Council and of the advisory committee to the Ministry of Health; practiced general medicine from 1892 to 1927; mayor of the borough of Hornsey, 1895-1896, and alderman till 1930; died at his home in Yeovil, Somerset, England, March 10, aged 76.

Government Services

Mobile Unit Used in Industrial Hygiene Service

The mobile unit of the Division of Industrial Hygiene of the National Institute of Health has just completed a survey covering fifteen plants and eight states. The five plants surveyed in Alabama top the number for any individual state. Three plants in Arkansas were included, two in Louisiana and one each in Mississippi, West Virginia, Kentucky, Oklahoma and Tennessee. A physician and an engineer were in charge of the survey.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Feb. 14, 1942.

An Official Medical History of the War

The work of compiling an official medical history of the war has begun. An editorial board under the chairmanship of the president of the board of education and composed of representatives of the fighting services, the Ministry of Health, the Department of Health of Scotland, the Committee of Imperial Defense and the Medical Research Council has been set up by the war cabinet to direct the preparation of a medical history of the war. This board will have the active collaboration of authoritative bodies and experts. They have met and discussed the scope and plan of the undertaking, the value of such a record made during the war and the war's contribution to medical science. Sir Arthur MacNalty, recently chief medical officer of the Ministry of Health, has been appointed editor in chief, and representatives have been appointed by the service departments concerned. The collection and classification of material has already begun. Much material on medical wartime problems exists and, of course, will grow as the war progresses. The editorial board hopes for the full support and cooperation of the medical profession and requests copies of published articles, reports and other information from health officers and physicians which may be of use in assembling material for the medical historians. They are invited to send it to the Editor in Chief, Medical History of the War, Room 208, Caxton House West, Tothill Street, London, S.W. 1.

The Sprue Syndrome

In *Guy's Hospital Reports* Sir Arthur Hurst describes an important advance which unifies the pathogenesis of the two sprue diseases and celiac disease. He points out that three constant and characteristic features are common to sprue, nontropical sprue and celiac disease and they require explanation in any theory explaining their pathology: 1. The stools contain an excess of split fat but no excess of neutral fat, meat fibers or starch, and no inflammatory material. 2. Roentgenography shows disappearance of the normal feathery or herring bone aspect of the duodenum and jejunum due to the valvulae conniventes. 3. No pathologic changes are found in the intestine after death if postmortem changes have been prevented. Under adequate treatment normal absorption of fat is restored with normal roentgenographic appearances. Hurst therefore concludes that tropical sprue, nontropical sprue and celiac disease are varieties of the same disorder—"the sprue syndrome"—and differ only in the part of the world in which the disease originates and the age of the patient. The characteristic features of the sprue syndrome are the result of paralysis of the muscularis mucosae, which would lead to loss of the pumping action of the villi, by means of which fat is conveyed from the lacteal radicles of the villi into the larger lacteals and to flattening of the valvulae conniventes without changes in normal appearance of the mucous membrane. Paralysis of the muscularis mucosae may be secondary to loss of the normal stimulant of Meissner's (submucosal) plexus or to the effect of vitamin deficiency or some toxemia on the plexus. An exception must be made for those cases of the sprue syndrome associated with disease of the mesenteric glands. Here the hindrance to fat absorption occurs at the level of the mesenteric glands instead of in the villi.

The Danish physician T. E. H. Thaysen previously (1932, 1935) gave good reasons for regarding sprue, nontropical sprue and celiac disease as varieties of the same disease. Celiac disease differs from sprue only in showing characteristics depending on its occurrence in young and growing children. There is no difference between celiac disease in European children whether it develops in the tropics, when it is likely to be called sprue, or in Europe, or between tropical and so-called nontropical sprue. As Thaysen has pointed out, the tendency to regard diseases more common in the tropics as differing fundamentally from similar ones occurring in nontropical countries is quite unjustifiable. It has gradually been recognized that true beriberi occurs in England and even in Iceland and Newfoundland as well as in hot climates whenever the essential dietetic deficiency is present. The same holds for pellagra, which was long regarded as a purely tropical disorder. Thaysen gave the name idiopathic steatorrhea to the group of diseases comprising sprue, nontropical sprue and celiac disease. But this does not give any indication that the steatorrhea consists in the excretion of split fat in the excretion form of fatty acids and soaps and not of neutral fat.

Canadian Orthopedic Unit for Scotland

An appeal to Canada to send an orthopedic unit for service in the Scottish emergency hospitals has met with a prompt response. Nine Toronto orthopedists and twenty-two nurses experienced in orthopedic work and chosen from all parts of the dominion have arrived with the latest contingent of Canadian soldiers. They brought some special equipment, the gift of the Canadian Red Cross Society, which, with the Canadian Medical Association, organized the unit. The unit is led by Dr. Le Mesurier of the Toronto Sick Children's Hospital and Miss A. B. Hunter, who was matron at Port Arthur General Hospital. Dr. Andrew Davidson, chief medical officer for Scotland, who welcomed the unit, said that before the war Scotland had inadequate provision for orthopedic surgery; now it had the makings of a first class scheme not only for the present emergency but for the postwar period.

The Vitamin D Added to Margarine to Be Doubled

In the last great war the margarine, which then, as now, largely replaced butter, left much to be desired. It was not vitaminized and had a vile taste. Now the taste is so good that few can distinguish it from butter, which it is claimed to equal in vitamin content. It is announced that the amount of vitamin D added to margarine is to be doubled and that in future an ounce will contain more of the vitamin than an average egg. Vitamin D is specially important for children because of its part in the forming of bones and teeth. The other principal sources of vitamin D are eggs and cod liver oil. Increasing advantage is being taken of the free distribution of the oil. But whether the addition of synthetic vitamins to margarine makes it equal to butter has been questioned by Prof. J. C. Drummond, scientific adviser to the Ministry of Food, as stated in a previous letter. He holds that our knowledge of vitamins is still imperfect, that there may still be factors in our natural foods besides those which are replaced by synthetic vitamins.

Acute Hemorrhagic Pancreatitis as a Cause of Sudden Death

The symptoms of acute pancreatitis are generally compared to those of perforation of the stomach or intestine, but the shock and pain are stated to be even more intense. Yet, while sudden death is recognized as a rare result of perforation, this is unmentioned in the textbook descriptions of acute pancreatitis and does not appear to have been reported in British journals previously. Dr. J. F. Gaskell, physician to Addenbrooke's Hospital, Cambridge, has recorded in the *Clinical Journal* for January 10 cases of sudden death due to acute hemorrhagic pancreatitis which have come under his observation since December 1932 in necropsies performed by order of the coroner. The subjects were apparently in normal health within two hours of being found dead, except when death had taken

place in bed at night. The evidence that acute pancreatitis was the cause of the sudden death is the condition of the pancreas, with failure, except in one case, to discover any other possible cause. The pancreas was softer than normal and showed hemorrhages in its substance round the ducts and vessels. Fat necrosis was found microscopically, but the macroscopic evidence was slight, which Dr. Gaskell explains by the fact that the death was too sudden to allow it to develop. How dramatic the cases were in their suddenness is shown by the case of a Cambridge undergraduate aged 22, who went on a hare and hound run almost directly after a heavy meal. He stopped about a mile away and bent forward with his hands on his abdomen. He sat in a hedge and was left by a friend, who thought that he was winded. Others in the run coming up later found him dead. The necropsy showed acute hemorrhagic pancreatitis. The pancreas was swollen and tinged pink throughout and microscopically was entirely necrosed with hemorrhages round the vessels.

Streptococcic Cross Infection in Hospital Wards

Recently the danger of wounds becoming infected in hospital wards has been recognized. At a meeting of the Section of Surgery of the Royal Society of Medicine the president, Mr. E. Rock Carling, said that surgeons had been slow in appreciating the work on cross infection done by physicians in hospitals for infectious diseases but that shortly before the war much work was done in wards and operating rooms in the study of the bacterial content of the air and in attempts to sterilize the air by aerosols or ultraviolet rays. Some of the results were startling. Perhaps it was not surprising that in the course of bronchoscopy bronchial flora should in a few minutes be recovered from a distant part of the operating room, but it was surprising that air hitherto entirely free from Bacillus pyocyaneus should be found to contain it within five minutes of opening an abscess in which it was present. After Dunkirk surgical literature became full of more extended investigations, and a group of pathologists put forward a new technic for war dressings (THE JOURNAL, Nov. 15, 1941).

Prof. A. A. Miles said that the organism commonly concerned in cross infection in wards, Streptococcus pyogenes, was most easily traced. It was not the commonest cross infecting organism but, owing to its pathogenicity, the most important. In the peacetime surgical ward the streptococcus reservoir was mainly in the upper respiratory tract. In war additional reservoirs were wounds infected before admission, and hospital infection was more common. The three main channels of infection—dust, droplets and hands and instruments—demanded separate precautions. They could be divided into those in the technic of wound dressing and those apart from it. An improved "no touch" technic with rigid separation of the duties of the dressing team and special precautions against the carrying of infection from bed to bed had substantially reduced hospital infection.

Prof. J. Paterson Ross described the essentials of good technic as follows: 1. Precautions against contamination by dust: bed making to be completed an hour before dressings began; lids for dishes and buckets; wounds to be exposed for only a minimum time. 2. Precautions against contact infection: fingers never to touch a wound, skin around or dressings next the skin; forceps to be used or gloves worn; hands and instruments to be dry. 3. Methods of sterilization: instruments and accessories for dressing to be sterilized by effective methods; cleaning of baths to be beyond reproach.

Dr. M. van den Ende said that bacteria were carried through the air in droplets or dust particles. Large droplets carrying infective doses had a relatively short range and fell to the ground rapidly. Adequate bed spacing and masking was the most effective method of dealing with them. Dry dust borne organisms were distributed into the air in large numbers during bed making and floor sweeping and might remain suspended for long periods. They could be reduced by treating floors and bedclothes with dust laying oils.

Sir James Walton said that in this war, in contrast to the last war, there had been little experience with gross infections. Bomb lacerations were operated on as soon as the patients got over the shock. If possible, the wounds were sewn up and a dressing was put on which was not removed for ten days, and then complete healing was found. If the wounds were large they were packed with petrolatum gauze, which was not touched for three or four days. Ever since the last war he had been teaching that dressers should use only forceps and should touch nothing with the hand.

London's Underground Railway as a Refuge

Remarkable figures are given of the part played by London's underground railway system as a place of refuge from air raids. During 1941, sixteen million people were given shelter at seventy-nine underground stations. Eight and a half miles of three tier bunks were installed on platforms and subways. Canteens for the refugees were provided, and 11 tons of food was distributed nightly during the raids. Other war measures were also taken by the Transport Board. Three hundred and eighteen thousand four hundred yards of netting was put on vehicle windows to protect passengers from glass broken by blast. Nine thousand five hundred women workers displaced men on the railway. Two thousand three hundred allotments of 80 acres were cultivated for the growing of food by the railway employees.

RIO DE JANEIRO

(From Our Regular Correspondent)

Jan. 25, 1942.

Medical Advertising Regulated by Law

There is no medical association in Brazil with the significance and functions corresponding to those of the American Medical Association in the United States. There are many local medical societies, and in Rio de Janeiro there is the National Academy of Medicine; but a system of affiliation of the local associations into a central national organization is completely lacking. In a country larger than continental United States and insufficiently provided with means of communication, these local medical societies are completely separated from one another. Thus there is no uniformity of policies, no ideas in common, and in certain cases there is even some antagonism. The lack of a central professional body to establish policies explains the diversity of attitudes of separated groups of physicians, the variable behavior of the practitioners and the diversified ethical codes which they follow. Consequently it is not uncommon for many physicians to indulge in extensive advertising, use academic and professional titles to which they are not entitled, try to deceive patients with promises of cure that cannot be fulfilled, and boast special systems of medicine that in some instances border on quackery.

To remedy this situation, federal legislation has been enacted attempting to regulate medical advertising. This act forbids physicians to advertise (1) the cure of certain diseases for which there is no established treatment, (2) treatments aiming to control or to interrupt pregnancy, (3) the practice of more than two medical specialties, (4) treatments through correspondence and newspapers or over the radio, (5) the practice of a medical specialty not included in the curriculum of medical schools and the reference to methods of diagnosis and of treatments not yet recognized by the medical societies, (6) the practice of nonpaid consultations in private offices, (7) discrediting references to systems of medicine and to therapeutic procedures recognized by the present legislation and (8) testimonials or statements from patients certifying the cure of diseases for which there is no established treatment. The act permits the physician to

advertise his academic and scientific titles or real professional qualifications, the price of his services and a general reference to the resources and appliances he uses, as x-rays, radium or medical electricity. It is also permissible to use the press or the radio to discuss medical and health problems in a general manner, without the character of individual treatment. Another section of the same act is intended to control the exaggerations used in the advertising of "patent medicines" and proprietary drugs. It is forbidden to advertise these drugs in the lay press (1) without the declaration "to be sold only under medical prescription" if this condition has been imposed in the licensing of the drug, (2) with the claim to cure tuberculosis, syphilis, cancer or blennorrhagia, (3) with the support of statements from lay patients that they have been cured, (4) with the claim to control or to interrupt pregnancy, (5) with discrediting references to the climate or to the sanitary conditions of the country and (6) with pictures to exhibit physical deformities or obviously faked illustrations to deceive the public.

Leprosy in Brazil

Leprosy is an important health problem in Brazil, because of the large absolute number of cases and the slightly increasing trend. The earliest reference to the disease in this country is from Sa Menezes in 1696. Saint-Hilaire described cases of leprosy in 1820 in the state of Minas Gerais. Prior to 1920 there was no special organization to combat leprosy in Brazil. In that year Carlos Chagas created the division of leprosy in the Brazilian Public Health Service, and Prof. Eduardo Rabello was put in charge of that division. At that time about 20,000 cases of leprosy were supposed to exist in Brazil. The first work of the new division of leprosy was to establish centers of diagnosis throughout the country. Ten years later the number of lepers was estimated by Rabello and Silva Araujo to be about 30,000. Dr. Ernani Agricola, now in charge of the division of leprosy, estimates that the present number of lepers is at least 45,000, or about 100 per hundred thousand of population. According to the leprologist Muir, in the whole world the bulk of the patients are in Asia and Africa (China 1 million, India 1 million, Africa about half a millon). The prevalence of leprosy in Brazil is comparable to that of Russia, which has about 170,000 lepers to 170 million of population. The most recent statistics place the number of lepers in the Americas at below 100,000. The estimated distribution is, however, most irregular, and the figures are repeatedly being revised upward.

There are now sixteen modern leprosariums in Brazil, where 15,173 patients were isolated, Dec. 31, 1941. In the state of São Paulo more than 90 per cent of the contagious cases are isolated in six leprosariums. About 2,500 cases are isolated in the state of Minas Gerais and about 1,000 in the state of Para. There are fifteen preventoriums where nondiseased children of lepers are interned, and many more institutions are in course of organization. Many centers of treatment are in operation. where chaulmoogra oil is used extensively. Since 1938 the technic of infiltration of the lesions, through multiple local injections of chaulmoogra oil, has been increasingly used, with promising better results. The raw chaulmoogra material has been imported from India, and the chemical division of the Oswaldo Cruz Institute refines this material and prepares three different kinds of chaulmoogra derivatives. The Brazilian personnel of the institute has been trained by an American specialist, Dr. Howard Cole. The institute is trying to prepare therapeutic material from Brazilian plants of the genus Hydnocarpus. Extensive studies on the biology of the leprosy bacillus have been carried out in the Oswaldo Cruz Institute by Dr. H. C. Souza Araujo, who knows the problem of leprosy from direct observation in about forty countries of the world. The epidemiology of leprosy in Brazil is also now under investigation. About 25 per cent of the cases are of the pure nervous form. The disease is more prevalent in males than in females, and also more prevalent in colored natives than in white Brazilians. The prevalence is higher in white foreign people and in white foreign born Brazilians than in white native born Brazilians.

Brazilian Council of Ophthalmology

As a result of the decision of the fourth Brazilian Congress of Ophthalmology, held in Rio de Janeiro in July 1941, the Brazilian Council of Ophthalmology has been founded. The chief functions of the council are (1) to promote the development and progress of the specialty in Brazil and to establish standards of fitness to practice ophthalmology, (2) to act as preceptors for prospective students of ophthalmology and (3) to arrange and conduct examinations to test the qualifications of those who practice ophthalmology and desire a certificate to prove that they meet the standards established by the council. The council will be formed by the professors of ophthalmology from the medical schools of Rio de Janeiro, São Paulo, Bahia, Porto Alegre, Recife and Bello Horizonte and the presidents of the Brazilian Association of Ophthalmology and of four other state ophthalmologic associations. There will be a central executive board and a regional board in each one of the twenty states of Brazil. Examinations will be held annually and will include the applicant's professional and ethical record (at least two years of private practice), at least twenty case reports and a written examination. The constitution of the council permits, as an introductory measure, that the certificate be issued, up to June 30, 1942, to the physicians who prove that they have had a private practice of ophthalmology of at least five years, or at least two years of practice if they prove the completion of an internship of ophthalmology of not less than one year, or to the physicians who are at present ophthalmologists of hospitals, of clinics and of federal, state or municipal health organizations.

Marriages

MERVYN SHOOR, Lieutenant (j. g.), Medical Corps, U. S. Navy, to Miss Enid Olivi of San Francisco, at Mare Island, Calif., Oct. 25, 1941.

ANGUS CRAWFORD RANDOLPH, Lynchburg, Va., to Miss Marjorie Armstrong McLernon of San Antonio, Texas, Dec. 20, 1941.

HAWLEY HOWARD SEILER, Paia, Maui, Hawaii, to Mlle. Marie Augusta Schreiber of Paris, France, Oct. 4, 1941.

RALPH SILER MORGAN, Durham, N. C., to Miss Ruth Evelyn Dodd of Asheville in Arden in December 1941.

RICHARD A. FORNEY, Rochester, Minn., to Miss Margaret Magel of Twin Falls, Idaho, Aug. 28, 1941.

IGNATIUS W. MADURA to DR. EDITH EASON, both of Chicago, at North Bend, Neb., Dec. 20, 1941.

CLEMENT W. BYRNES to Miss Nona Jane Moore, both of Dunlap, Iowa, in St. Louis, Dec. 23, 1941.

ANTHONY RALPH MARSICANO, Brooklyn, to Miss Marion Elizabeth Hobbs of Macon, Dec. 25, 1941.

PHILIP CARY WHITEHEAD, Chatham, Va., to DR. BETTY GORDON WILLIS of Culpeper, Dec. 25, 1941.

FREDERICK MARTIN GRAHAM to Miss Elizabeth Braasch, both of Rochester, Minn., Nov. 15, 1941.

ARTHUR C. LAWRENCE, Lincoln Park, N. J., to Miss Evelyn H. Abrash of Paterson, Nov. 30, 1941.

EDMOND H. KALMON JR., Albany, Ga., to Miss Marion Binkley at Nashville, Tenn., Dec. 2, 1941.

MASON C. SMITH, Meriden, Miss., to DR. ELVIRA A. CORRALES of Tampa, Fla., Dec. 29, 1941.

ARTHUR F. GRANDINETTI, Davenport, Iowa, to Miss Rose Tomlin of Waterloo, Dec. 29, 1941.

WILLIAM M. KUNTZ, Columbus, Ohio, to Miss Mertes Mudd of Waco, Texas, Dec. 30, 1941.

GEORGE C. MCCALLUM, Portland, Ore., to Miss Ruth Waind of McMinnville, Dec. 27, 1941.

ROBERT HAYTER, Dallas, Ore., to Miss Joan Schuyler of Tacoma, Wash., Dec. 5, 1941.

Deaths

Frank Frazier Hutchins, Indianapolis; Medical College of Indiana, Indianapolis, 1892; member of the Indiana State Medical Association and the National Committee for Mental Hygiene; instructor at the Butler University Medical Department and the Indiana Medical College from 1892 to 1895; assistant professor of psychology and psychiatry at the Central College of Physicians and Surgeons from 1903 to 1905; professor of mental and nervous diseases at the State College of Physicians and Surgeons from 1906 to 1908; professor of mental and nervous diseases at the Indiana University School of Medicine from 1908 to 1937 and since 1937 emeritus professor; served as a lieutenant colonel during World War I; at one time medical director and superintendent of the Marion (Ind.) National Sanatorium; formerly chief of the neuropsychiatric service at the Walter Reed General Hospital in Washington, D. C.; clinical director of neuropsychiatry at the United States Veterans' Bureau from June 1922 to July 1923, and formerly dean of the school of neuropsychiatry; colonel in the medical reserve corps of the United States Army; consultant to the City Hospital, Robert W. Long Hospital and the James Whitcomb Riley Hospital for Children; aged 71; died, February 22, in the Methodist Hospital of cerebral hemorrhage.

Martha Tracy ✠ Philadelphia; Woman's Medical College of Pennsylvania, Philadelphia, 1904; since 1940 assistant director of public health of Philadelphia; was associated with her alma mater since 1907 as associate professor and director of the laboratory of physiologic chemistry from 1907 to 1913, professor of physiologic chemistry from 1913 to 1921, professor of hygiene from 1921 to 1923, professor of preventive medicine from 1923 to 1931, dean from 1917 to 1940 and since 1940 emeritus dean; worked with the research department of experimental pathology at Cornell University Medical College, New York, from 1904 to 1907, and for many years under the Huntington Fund for Cancer Research, New York; formerly a member of the board of health of Philadelphia and director of the Philadelphia health council and tuberculosis committee; fellow of the American College of Physicians and of the College of Physicians of Philadelphia; past president of the American Medical Women's Association; in 1917 was awarded the doctor of public health degree from the University of Pennsylvania, Philadelphia; aged 65; died, March 22, in the Hospital of the Woman's Medical College of pneumonia.

James Addison Price ✠ Memphis, Tenn.; Atlanta (Ga.) College of Physicians and Surgeons, 1912; past president of the Tennessee Tuberculosis Association; formerly vice president of the National Tuberculosis Association; served during World War I; at one time assistant professor of medicine at the University of Tennessee College of Medicine; superintendent of the Irene Byron Sanatorium, Fort Wayne, Ind., from 1919 to 1921; from 1921 to 1941 medical director of the Oakville (Tenn.) Memorial Sanatorium; was on the staffs of the Methodist Hospital, John Gaston Hospital and the Baptist Memorial Hospital, where he died, January 10, of cerebral hemorrhage, aged 54.

Harry Arthur Paskind ✠ Chicago; University of Illinois College of Medicine, Chicago, 1920; associate professor of nervous and mental diseases at Northwestern University Medical School; member of the American Neurological Association, Association for Research in Nervous and Mental Diseases and the Central Neuropsychiatric Association; president of the Chicago Neurological Society, 1940-1941; served during World War I; editor of the psychiatric section of the *Year Book of Neurology, Psychiatry and Endocrinology* from 1934 to 1938; aged 45; attending neurologist, Evanston (Ill.) Hospital, where he died, March 24, of bronchiectasis and cardiac hypertrophy.

Arnold R. Miller, Harrisville, Mich.; Detroit College of Medicine, 1906; member of the Michigan State Medical Society; past president of the Alpena County Medical Society; for many years mayor of Harrisville; member of the board of education; chairman of the Civilian Defense Council and an examiner for the county draft board; at one time acting assistant surgeon in the United States Public Health Service; owner of a hospital bearing his name; aged 59; died, February 22, of injuries received in an automobile accident.

R. Andral Bratton, York, S. C.; Medical College of the State of South Carolina, Charleston, 1884; member of the South Carolina Medical Association; past president of the York County Medical Society; formerly member of the state board of medical examiners; for many years a member of the board of trustees of the city schools; on the visiting staff of the York County Hospital, Rock Hill; aged 82; died, January 26, of arteriosclerosis.

Harry Louis Pollock ✠ Chicago; College of Physicians and Surgeons of Chicago, 1894; member of the American Academy of Ophthalmology and Otolaryngology and the American Laryngological, Rhinological and Otological Society; fellow of the American College of Surgeons; head of the department of otolaryngology, American Hospital; on the staff of the Walther Memorial Hospital; aged 67; died, January 24, in Los Angeles.

Alfred Jones Drury ✠ Roselle, N. J.; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1923; member of the Medical Society of New Jersey; on the staffs of the Elizabeth General Hospital and St. Elizabeth Hospital, Elizabeth, N. J., and the Rahway (N. J.) Hospital; physician for the public schools; aged 44; died, January 24, of coronary thrombosis.

Nathan Goodfriend ✠ New York; Columbia University College of Physicians and Surgeons, New York, 1902; fellow of the American College of Surgeons; attending ophthalmologist, Bronx Hospital, and secretary of its medical board; assistant surgeon, Manhattan Eye, Ear and Throat Hospital; aged 61; died, January 17, of coronary thrombosis.

Frank Edgar Fee ✠ Cincinnati; Medical College of Ohio, Cincinnati, 1895; professor emeritus of clinical surgery at the University of Cincinnati College of Medicine; fellow of the American College of Surgeons; visiting surgeon, Christ Hospital; consulting surgeon, Cincinnati General Hospital; aged 68; died, January 29, of coronary occlusion.

Ambrose Watts Thrush, Chambersburg, Pa.; Jefferson Medical College of Philadelphia, 1890; member of the Medical Society of the State of Philadelphia; secretary and past president of the Franklin County Medical Society; formerly county coroner; aged 76; on the staff of the Chambersburg Hospital, where he died, January 28, of pneumonia.

W. Kempton Browning, Merchantville, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1897; member of the Medical Society of New Jersey; served as medical inspector in the schools of Camden and Merchantville; aged 67; died, January 22, in the Cooper Hospital, Camden, of coronary occlusion and lobar pneumonia.

Charles Harkness Willits, Miami, Fla.; University of Pennsylvania Department of Medicine, Philadelphia, 1879; medical director of the Provident Mutual Life Insurance Company in Philadelphia; aged 84; died, January 2, of aortic stenosis and chronic cystitis.

Bertrum Brant McElhany ✠ Youngstown, Ohio; Western Reserve University Medical Department, Cleveland, 1900; on the consulting staff of St. Elizabeth Hospital; aged 69; died, January 13, in the Youngstown Hospital, Southside Unit, of injuries received when struck by an automobile as he was crossing the street.

Oat Whitney ✠ Adrian, Mich.; Michigan College of Medicine and Surgery, Detroit, 1894; past president and secretary of the Lenawee County Medical Society; on the staff of the Emma L. Bixby Hospital; aged 73; died, January 7, in the Harper Hospital, Detroit, of primary splenic anemia and pyelonephritis.

Frederick Chalfonte Peters, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1911; served during World War I; since 1939 professor and head of the department of ophthalmology at his alma mater; aged 54; died, January 7, in the Hahnemann Hospital of intracranial hemorrhage.

David Arthur Morgan, Memphis, Tenn.; Barnes Medical College, St. Louis, 1905; served during World War I; at one time on the staff of the United States Veterans Hospital, Excelsior Springs, Mo.; aged 58; died, February 23, in the Baptist Memorial Hospital of cerebral hemorrhage.

John Adams Miller, Roscoe, N. Y.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1887; member of the Medical Society of the State of New York; for many years county coroner; aged 79; died, January 17, in Monticello of chronic myocarditis.

Samuel Mathew McLaughlin, Santa Monica, Calif.; Eclectic Medical Institute, Cincinnati, 1899; served during World War I; aged 68; was shot and killed, January 18, when he was driving past an aircraft plant and the gun of a soldier who was on guard was accidentally discharged.

Gertrude Anna Spriggs, Lomita, Calif.; College of Physicians and Surgeons of San Francisco, 1900; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1903; member of the California Medical Association; aged 77; died, Dec. 30, 1941.

Daniel Crumlish Handley, Cincinnati; Cincinnati College of Medicine and Surgery, 1897; member of the Ohio State Medical Association; at one time county and deputy coroner; served during World War I; aged 73; died, January 30, in Christ Hospital of uremia.

Charles Joseph Jaquish, Houston, Texas; University of Pennsylvania School of Medicine, Philadelphia, 1920; member of the State Medical Association of Texas and of the American Academy of Ophthalmology and Otolaryngology; aged 50; died, Dec. 24, 1941.

Charles Hayes King, Bucyrus, Ohio; Ohio Medical University, Columbus, 1906; member of the Ohio State Medical Association; past president and secretary of the Crawford County Medical Society; aged 63; died, January 29, of cerebral hemorrhage.

Henry John Niebruegge, St. Louis; St. Louis College of Physicians and Surgeons, 1900; member of the Missouri State Medical Association; on the staff of the Deaconess Evengelical Home and Hospital; aged 68; died, January 13, of heart disease.

Peter Albert Trice, Thomasville, Ala.; Louisville (Ky.) Medical College, 1902; member of the Medical Association of the State of Alabama; aged 67; died, January 14, in the Goldsby King Memorial Hospital, Selma, of cerebral hemorrhage.

George Francis Pierrot ✦ Seattle; American Medical College, St. Louis, 1889; St. Louis College of Physicians and Surgeons, 1890; formerly health officer of Wahkiakum County, Wash., and Eldorado County, Nev.; aged 80; died, Dec. 9, 1941.

Watson Fuller Wood, White Church, Kan.; University Medical College of Kansas City, Mo., 1891; member of the Kansas Medical Society; aged 81; died, January 20, in the Bethany Hospital, Kansas City, of cerebral hemorrhage.

Thomas Shaw Webster, Toronto, Ont., Canada; Victoria University Medical Department, Coburg, 1888; University of Toronto Faculty of Medicine, 1889; one of the founders of the Toronto Western Hospital; aged 84; died, Dec. 30, 1941.

David Herman Fuller, Fall River, Mass.; Jefferson Medical College of Philadelphia, 1904; formerly medical director and superintendent of the Fall River General Hospital; aged 61; died, January 31, in Westboro of meningoencephalitis.

Ernest Lafayette Handley, Pocahontas, Ark.; Kansas City (Mo.) College of Medicine and Surgery, 1920; member of the Arkansas Medical Society; formerly county coroner; aged 48; died, Dec. 9, 1941, in a hospital at Jonesboro.

Henry Albert Pfeifer, Milwaukee; Wisconsin College of Physicians and Surgeons, Milwaukee, 1909; member of the State Medical Society of Wisconsin; aged 59; died, January 12, in St. Joseph's Hospital of cirrhosis of the liver.

Edward M. Harris, Cushing, Okla.; Chattanooga (Tenn.) Medical College, 1901; member of the Oklahoma State Medical Association; aged 69; died, January 26, in the Oklahoma City General Hospital of diabetes mellitus and thrombosis.

Emerson Meadows Cooper, Rockwood, Mich.; Trinity Medical College, Toronto, Ont., Canada, 1900; member of the Michigan State Medical Society; aged 65; died, January 29, in the University Hospital, Ann Arbor, of uremia.

Lafayette Franklin Shoemaker, Hillsboro, Texas; Medical College of Alabama, Mobile, 1902; member of the State Medical Association of Texas; aged 73; died, Dec. 22, 1941, in a hospital at Temple of cerebral hemorrhage.

Albert Louis Gustetter ✦ Tucson, Ariz.; Medical College of Ohio, Cincinnati, 1900; past president of the board of medical examiners; veteran of the Spanish-American and World wars; aged 65; died in January of pneumonia.

Frank Terry Brooks, Palma, Majorca, Spain; Long Island College Hospital, Brooklyn, 1893; aged 73; died, January 12, in the Hospital of the Good Samaritan, Los Angeles, of arteriosclerosis, heart disease and diabetes mellitus.

Walton Wheeler Young, Washington, D. C.; Howard University College of Medicine, Washington, 1921; aged 65; died, January 6, in the Eastern Dispensary and Casualty Hospital of myocarditis and arteriosclerosis.

Lincoln Jay Pierce, Brookfield, Mo.; National University of Arts and Sciences Medical Department, St. Louis, 1913; member of the Missouri State Medical Association; aged 56; died, January 22, of mesenteric thrombosis.

Donald John Macdonald, Halifax, N. S., Canada; McGill University Faculty of Medicine, Montreal, Que., 1897; served during World War I; fellow of the American College of Surgeons; aged 69; died, Dec. 19, 1941.

Joseph J. Shafer ✦ Louisville, Ky.; Southern Medical College, Atlanta, 1897; member of the American Academy of Ophthalmology and Otolaryngology; aged 70; died, January 4, in St. Anthony's Hospital of pneumonia.

R. J. Clower, Morven, Ga.; Atlanta Medical College, 1895; member of the Medical Association of Georgia; aged 68; died, January 12, in the Brooks County Hospital, Quitman, of coronary occlusion and chronic nephritis.

Francis Marion Thurmon, Pearl, Ill.; Barnes Medical College, St. Louis, 1904; member of the Illinois State Medical Society; formerly mayor and member of the school board; aged 69; died, January 14, of uremia.

William W. Long, Sulphur Springs, Texas; Memphis (Tenn.) Hospital Medical College, 1901; member of the State Medical Association of Texas; aged 71; died, January 11, in Dallas of coronary sclerosis.

Andrew Hunter ✦ McKeesport, Pa.; Medico-Chirurgical College of Philadelphia, 1891; served during World War I; on the staff of the McKeesport Hospital; aged 72; died, January 23, of hypernephroma.

Frederick Kent Ream, Palm Beach, Fla.; Rush Medical College, Chicago, 1892; also a dentist; aged 72; died, January 18, in the Good Samaritan Hospital, West Palm Beach, of a self-inflicted bullet wound.

John H. O'Dell, Three Rivers, Mich.; Detroit College of Medicine, 1903; member of the Michigan State Medical Society; on the staff of the Three Rivers Hospital; aged 63; died, January 29, of pneumonia.

Norman Paull Hersam ✦ Stoneham, Mass.; Harvard Medical School, Boston, 1912; school physician; aged 57; died, January 15, in the Middlesex County Sanatorium, Waltham, of miliary tuberculosis.

Sidney Bruce Matthews, Winnfield, La.; Memphis (Tenn.) Hospital Medical College, 1911; aged 68; died, January 18, in a hospital at Shreveport of arteriosclerosis and hypertensive cardiovascular disease.

Moses Lot Haning, Browning, Mo.; St. Louis University School of Medicine, 1903; member of the Missouri State Medical Association; aged 63; died, January 9, in Muskogee, Okla., of coronary occlusion.

Fred V. Watson ✦ Los Angeles; Marion-Sims College of Medicine, St. Louis, 1899; on the staff of the Presbyterian Hospital-Olmstead Memorial; aged 65; died, January 6, of cerebral hemorrhage.

Charles Terrel Hughes, Gainesville, Texas; Kentucky School of Medicine, Louisville, 1889; member of the State Medical Association of Texas; aged 81; died, January 15, of cerebral hemorrhage.

Anthony Lothar Fink, Carroll, Iowa; Deutsche Universität, Medizinische Fakultät, Prague, Austria, 1910; on the courtesy staff of St. Anthony Hospital; aged 60; died, January 20, of chronic myocarditis.

Myer Jerome Herschman ✦ Washington, D. C.; George Washington University School of Medicine, Washington, 1917; member of the American Urological Association; aged 47; died, Nov. 15, 1941.

George Robert Norman, Tulsa, Okla.; Birmingham Medical College, 1911; member of the Oklahoma State Medical Association; served during World War I; aged 56; died, January 21, of aortitis.

Henry Peronneau Brown, Lynchburg, Va.; University of Virginia Department of Medicine, Charlottesville, 1907; county coroner; aged 58; died, January 29, of shock following an automobile accident.

John B. Legnard, Houston, Texas; Northwestern University Medical School, Chicago, 1902; served during World War I; aged 66; died, January 4, in the Hermann Hospital of coronary occlusion.

Huldah Davis Hurst, Lincoln, Neb.; Lincoln Medical College of Cotner University, 1905; aged 78; died, January 17, in the Medical and Surgical Hospital, San Antonio, Texas, of coronary occlusion.

Harry **Fleisher Rentschler,** Reading, Pa.; Jefferson Medical College of Philadelphia, 1893; member of the Medical Society of the State of Pennsylvania; aged 72; died, January 4, of angina pectoris.

William Givin Rhoten, Wooster, Ohio; Medical College of Ohio, Cincinnati, 1900; formerly health officer of Wayne County; aged 67; died in January in Massillon of chronic myocarditis.

Ora **Alexander Johnson,** Kansas City, Mo.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1897; aged 69; died, January 26, of coronary occlusion and carcinoma of the prostate.

Henry **Bernard Hibbe** ✠ Dubuque, Iowa; State University of Iowa College of Medicine, Iowa City, 1922; aged 50; died, January 24, in St. Clare Hospital, Monroe, Wis., of cirrhosis of the liver.

Louis George Cucinotta, Brooklyn; Tulane University of Louisiana School of Medicine, New Orleans, 1931; on the staff of St. John's Hospital; aged 37; died, January 17, of coronary thrombosis.

Mary Elizabeth Burns, Fitchburg, Mass.; Woman's Medical College of Pennsylvania, Philadelphia, 1910; for many years school physician; aged 59; died, January 27, of coronary thrombosis.

Robert **Reid Berry** ✠ Union, S. C.; Medico-Chirurgical College of Philadelphia, 1901; on the staff of the Wallace Thomson Hospital; aged 64; died, January 23, of coronary occlusion.

Harry Jarrett ✠ Camden, N. J.; Jefferson Medical College of Philadelphia, 1887; aged 75; died, January 29, at his home in Moorestown of injuries received in an automobile accident.

Andrew Sargent, Hopkinsville, Ky.; Louisville Medical College, 1881 and 1883; formerly member of the city council and state legislature; aged 83; died, January 31, of diabetes mellitus.

Albert Franklin Adams, Reno, Nev.; Cooper Medical College, San Francisco, 1904; served during World War I; aged 62; died, January 16, of coronary occlusion and hypertension.

Levi E. Hinshaw, De Ruyter, N. Y.; Dunham Medical College, Chicago, 1902; formerly a lawyer; for many years health officer; aged 77; died, January 21, of pernicious anemia.

Merle S. Boyer, Philadelphia; Medico-Chirurgical College of Philadelphia, 1896; medical director of the National Accident and Health Insurance Company; aged 71; died, Dec. 10, 1941.

George Westveer, Grand Rapids, Mich.; Physio-Medical College of Indiana, Indianapolis, 1898; aged 74; died, January 18, in St. Mary's Hospital of perforating ulcer of the stomach.

Warren Brodie De Jernett, Commerce, Texas; Bellevue Hospital Medical College, New York, 1883; aged 82; died, January 31, in a hospital at Dallas of cerebral hemorrhage.

Alton **Bowie Reddick,** Sylvania, Ga.; University of Georgia Medical Department, Augusta, 1911; aged 55; died, January 13, in Atlanta following an operation on the lung.

Eliel **Grant Myrick,** Fairfield, Iowa; Keokuk (Iowa) Medical College, College of Physicians and Surgeons, 1904; aged 72; died, January 6, of myocardial insufficiency.

Columbus Huffaker, Chrisman, Ill.; University of Louisville (Ky.) Medical Department, 1905; aged 69; died, January 11, in a hospital at Kankakee of chronic myocarditis.

Leo **J. Drozniakiewicz,** Milwaukee; Milwaukee Medical College, 1907; member of the State Medical Society of Wisconsin; aged 60; January 20, of coronary thrombosis.

Hollie Bascum Wilson, Vicksburg, Miss.; Bellevue Hospital Medical College, New York, 1888; aged 82; died, January 10, of uremia and benign prostatic hypertrophy.

Lee **Otis Vickery,** Lena, Ill.; Loyola University School of Medicine, Chicago, 1919; member of the Illinois State Medical Society; aged 54; died, January 10, of uremia.

Warford Lash Nixon, Somerville, N. J.; Jefferson Medical College of Philadelphia, 1889; served during World War I; aged 74; died, January 20, of cerebral hemorrhage.

T. N. McMillan, Thomaston, Ala.; Medical College of Alabama, Mobile, 1895; aged 74; died, January 18, in the Baptist Hospital, Selma, of coronary thrombosis.

William F. Decker, Suffern, N. Y.; New York Homeopathic Medical College, New York, 1876; aged 86; died, January 25, in Newburgh of cerebral hemorrhage.

Gilbert Leonard Hagen, Minneapolis; Minneapolis College of Physicians and Surgeons, 1904; aged 83; died, January 27, of cardiac decompensation and hypertension.

James Oscar Hicks ✠ Victoria, Texas; Kentucky School of Medicine, Louisville, 1906; aged 61; died, Dec. 31, 1941, in the Victoria Hospital of diabetes mellitus.

John A. Pollard, Lynchburg, Va.; University of Louisville (Ky.) Medical Department, 1894; aged 68; died, January 24, of mitral stenosis and coronary thrombosis.

Alfred H. Tickell, Nevada City, Calif.; Southern Medical College, Atlanta, Ga., 1891; member of the California Medical Association; aged 77; died, January 28.

George Mortimer Wetherell, Adrian, Mich.; Niagara University Medical Department, Buffalo, 1886; aged 84; died, January 3, of cerebral hemorrhage.

Benjamin Lawrence Brigham, Tacoma, Wash.; College of Physicians and Surgeons, Baltimore, 1880; aged 83; died, January 30, of cerebral hemorrhage.

William James Houck ✠ Newark, N. J.; Medico-Chirurgical College of Philadelphia, 1899; aged 75; died, January 27, of cerebral hemorrhage.

Palmer E. Brandon ✠ Sioux Falls, S. D.; Northwestern University Medical School, Chicago, 1907; aged 64; died, January 21, of coronary thrombosis.

S. D. Smith, Byron, Ga.; College of Physicians and Surgeons, Baltimore, 1882; aged 85; died, January 3, in a hospital at Macon of bronchopneumonia.

Michael Joseph McAvoy, Baltimore; College of Physicians and Surgeons, Baltimore, 1900; aged 69; died, January 27, of cirrhosis of the liver.

Ocie Rush Peek, Hickory, Miss.; Mississippi Medical College, Meridian, 1907; aged 73; died, Dec. 17, 1941, in the Rush's Infirmary, Meridian.

Houston Rather, Dallas, Texas; Kentucky School of Medicine, Louisville, 1893; aged 80; died, January 15, in Los Angeles of arteriosclerosis.

Frank M. Gallagher ✠ Columbus, Ohio; College of Physicians and Surgeons, Baltimore, 1901; aged 70; died, January 16, of coronary occlusion.

Paul Acberus Phillips, Springfield, S. C.; Bellevue Hospital Medical College, New York, 1891; aged 72; died, January 23, of heart disease.

John Wesley Moorer, Selma, Ala.; Meharry Medical College, Nashville, Tenn., 1899; aged 62; died, January 12, of cardiac decompensation.

Benjamin Hooke Anderson, Andersonburg, Pa.; Medico-Chirurgical College of Philadelphia, 1899; aged 74; died, January 8, of senility.

Henry John Hunter, Ilion, N. Y.; Baltimore University School of Medicine, 1890; aged 73; died, January 2, of cerebral hemorrhage.

Burwell Wilks Gunn, Maplewood, Mo.; Marion Sims College of Medicine, St. Louis, 1892; aged 78; died, January 30, of myocarditis.

Frank Beemer, Toronto, Ont., Canada; Victoria University Medical Department, Coburg, 1884; aged 79; died, Dec. 12, 1941.

Abram C. Boice, Orange, Calif. (licensed in Indiana in 1897); aged 85; died, Dec. 29, 1941, of chronic myocarditis.

DIED IN MILITARY SERVICE

Benjamin Franklin Norwood ✠ Medical Director, Captain, U. S. Navy, New York; University of Tennessee College of Medicine, Memphis, 1912; entered the Navy Sept. 24, 1917; surgeon attached to the Naval Medical Supply Depot, Brooklyn; aged 56; died, January 12, of coronary thrombosis.

Adrian Collison Schoedel, Flushing, N. Y.; University and Bellevue Hospital Medical College, New York, 1934; member of the Medical Society of the State of New York; first lieutenant in the medical reserve corps of the United States Army, in the 3d Battalion, 18th Infantry, 1st Division, Fort Devens, Mass.; aged 32; was killed, February 17, in an automobile accident near Acton, Mass.

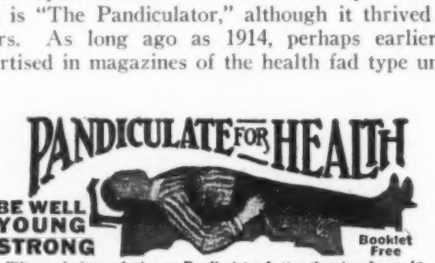
Bureau of Investigation

"MEDIEVAL RACK" STRETCHES THE TRUTH—NOT THE SPINE

U. S. P. O. Department Catches Up with the Pandiculator

So-called spine stretchers, advertised to increase height, "rejuvenate" or perform some other miracle, are so obviously fraudulent that the Post Office Department has banned one after another from the mails for the protection of the public. One of the early ones to suffer this fate—as long ago as 1914—was "The Cartilage Invention," which was promoted from Rochester, N. Y., by some notorious swindlers whose other medical schemes also were scotched by the Post Office. Other similar devices have been exposed in these pages during the intervening years, including one put out by Clara Louisa Glover and "Bernard Bernard" (real name Trapschuh, himself a short person) from Sausalito, Calif. (see THE JOURNAL, July 6, 1929, p. 53). Another similar swindle was the "Stebbing System of Height Increase," originally promoted from London, England, but later from the United States, by Mrs. Daisy Stebbing, along with a "Beautipon Treatment" for putting on weight and the "Slimcream Method" of reducing.

The latest "spine stretcher" to be branded by the Post Office as a fraud is "The Pandiculator," although it thrived for over thirty years. As long ago as 1914, perhaps earlier, it was being advertised in magazines of the health fad type under such


PANDICULATE FOR HEALTH
BE WELL
YOUNG
STRONG
Booklet Free
Fifteen glorious minutes on Pandiculator better than two hours in gymnasium. Refreshes, rejuvenates. Helps retain youth, energy, vigor, vim. Wonderful results. Doctors recommend it. No electricity, no discomfort; delightfully restful. Write for Free Booklet.
PANDICULATOR CO., 681 Hanna Bldg., Cleveland, Ohio

A typical "Pandiculator" advertisement.

claims as "Grow Tall! Get Well! Be Young . . . No More Rheumatism or Sciatica . . . A Cure for Old Age. It will Increase the Length of the Human Body." Further, it was claimed to have "gained the unqualified approval of the foremost physicians of all schools." Perhaps this meant merely the osteopathic school, for the testimonial of Albert Thurlow Hunt, an Omaha osteopath who later moved to Los Angeles, was especially featured. He put out a preposterous device of his own under the high sounding name "Dr. Hunt's New Cervical Spine Relaxer." This was so obviously fakish that the Post Office debarred it from the mails by means of a fraud order, as detailed in THE JOURNAL, Dec. 27, 1941, page 2269.

The few doctors of medicine whom The Pandiculator Company of Cleveland cited as users and endorsers of its device were persons of low professional standing such as Albert Abrams and George Starr White, whose own medicomechanical fakes often have been exposed in these columns. The Pandiculator concern brazenly circularized doctors of medicine with such claims as "Progressive leaders of the medical profession have accepted Pandiculation without reservation . . . There is no danger, no experimentation—Pandiculation is no theory. Practice has proved its merits and the medical profession has approved of its use. It is no fad or novelty which will evaporate over night." Nevertheless, the company deemed it expedient to call the device by different names according to the type of practitioner: "The Traction Couch for Physicians," "The Osteotractor for Osteopaths" and "The Chiro-tensor for Chiropractors." Nor were these various practitioners to have exclusive rights in employing it, for it was also played up "for home use by all the family." If there was any difference among these Pandiculators the theory and operation apparently were the same.

The Pandiculator was not cheap, at least in price, for a doctor of medicine who was solicited by form letter to purchase one was told that it would cost him $120—but then, the possession of it, he was informed, "opens the door of opportunity for you" and offered "an opportunity to take your place with leading members of your profession." "Inordinately gullible" would be the accurate substitution for "leading."

But Uncle Sam frequently is skeptical about promises that seem a bit too rosy. On May 29, 1941 the Post Office Department served notice on The Pandiculator Company of Cleveland and its officers to show cause on June 18 why a fraud order should not be issued against it. After the defendants had obtained several continuances the company's secretary, H. C. Crowell, and the firm's attorney appeared at the hearing finally held on August 6. At that time the government charged the Pandiculator Company with using the mails to promote its device by means of false and fraudulent pretenses, representations and promises to the effect that when used as directed it would prevent, overcome and cure "every conceivable condition and physical deficiency" including goiter, rheumatism, angina pectoris, pleurisy, asthma, tuberculosis, pneumonia, hay fever, ulcers, diabetes, Bright's disease, rupture, female disorders, locomotor ataxia and other ailments too numerous to catalogue here. All this regardless of the causes of these disorders or the failure of other methods of treatment to produce such results!

The hearing brought out that the Pandiculator Company was not a corporation in spite of its using the names of persons represented as its "officers"; that its sole owner was the person designated as "secretary," Henry C. Crowell, a Cleveland attorney; that Crowell had purchased the business in 1918 from a David B. Cropp and later had sold it to a Harry L. Spaulding, from whom he had bought it back in 1932, and that since then he had operated it for his sole use and benefit. According to his testimony approximately seven thousand Pandiculators had been sold to the public at prices ranging from $25 to $125. Some customers had purchased the device after assurance from the promoters that it would cure them of such diseases as tuberculosis, diabetes and arthritis. Some others had reported to the Post Office that the company neither filled their orders nor refunded their money, or, if it did the latter, it was only after complaint had been made to the Post Office.

According to other evidence presented, the Pandiculator sold to home users was a rectangular shaped box covered with fabrikoid. At the ends were T shaped iron posts, one of which was affixed to the box and the other to an adjustable bar which ran in under the box. To use the device a person had to recline on the box and attach his feet to the adjustable post and his head to the fixed post by means of straps which were part of the mechanism. Then, by turning a wheel on the side, which was attached to a cable threaded through a system of pulleys, the adjustable bar was extended and the body stretched.

An eminent orthopedic surgeon of Washington, D. C., who was called as an expert medical witness for the government testified that he had examined the Pandiculator and was familiar with its action and the effect it would have when used as directed; that this would be a stretching of the body but in only one direction, from head to foot; that spinal deformities caused by tuberculosis, syphilis, arthritis, rickets and infantile paralysis must be considered each on a separate and distinct basis in every instance; that although so-called traction therapy is sometimes used by orthopedists in treating certain diseases of the bones and joints, the direction and weight of the pull required in order to obtain beneficial results therefrom can be obtained only after a thorough examination of the patient by a competent practitioner; and that such examination frequently reveals that traction, even when indicated, must be exerted in an angular direction rather than in a straight line, as with the Pandiculator, and must be applied continuously rather than intermittently, as with this device. The witness also exposed the fallacy of some other representations made for the Pandiculator. The opposing witness was a chiropractor and naturopath.

The general worthlessness of the device for increasing height and curing or even benefiting the numerous ailments mentioned in the advertising was so apparent that a fraud order was issued on Dec. 8, 1941 debarring the Pandiculator Company and H. C. Crowell from the mails. Thus passes—it is hoped—a scheme that has swindled the credulous for many years.

NEW NAMES FOR OLD SWINDLES

Collecting Fraud Orders as a Hobby

Certain individuals against whom more than one Post Office Fraud Order has been issued were exposed under the above title in THE JOURNAL for March 7, 1942, p. 837. Others of a similar ilk are presented herewith:

"Prof." C. A. Isbell, Fred Mandeville, V. L. Mandeville and V. L. Davis.—This department of THE JOURNAL, Sept. 28, 1940, page 1118, dealt with fraud orders that the Post Office Department had issued against seven concerns for conducting medical swindles through the mails. One of these was operated by a "Prof." C. A. Isbell of Colfax, Calif., who promoted "Isbell's Mineral" for such disorders as cancer, diabetes, pyorrhea, rheumatism, hemorrhoids, stomach ailments and venereal diseases. And what was this alleged panacea? Just a mixture of iron and aluminum sulfates with minute amounts of silica, phosphate, calcium and potassium! Apparently reluctant to relinquish a profitable piece of quackery, Isbell attempted to evade the fraud order by advising his customers and prospects to send no *postal* money orders but to remit by checks or express money orders addressed to Fred Mandeville at Colfax, Calif. (Isbell's home town), or to V. L. Mandeville or V. L. Davis at Weimar, Calif. But the Post Office again caught up with Isbell and on Feb. 7, 1941, extended the 1940 fraud order to cover these Mandeville and Davis names.

Tru-Science, Natur-Tabs Company and Wilbur Hanson.—In THE JOURNAL Dec. 28, 1940, page 2298, there was described in detail a case in which the Post Office Department closed the mails on May 28, 1940 to the Natur-Food Company and its officers and agents at Kansas City, Mo. The article showed that this fraud order was supplemental to one that the Department had issued on Feb. 1, 1940 against the National Diabetik Food Company, George H. Keyes and R. Randall for conducting a fraudulent mail-order scheme in selling "National Diabetic Food" and a supplementary product, "National Mineral Ration" as an alleged "diabetes cure." After the issuance of the first fraud order the Department discovered that the scheme was being conducted under the name Natur-Food Company and hence found it necessary to issue an additional order. Further, the article brought out that National Diabetic Food was a pulverized form of the weed saltbush, and its ash contained traces of calcium, iron phosphate, sodium, potassium and chloride. It was further shown that National Mineral Ration was essentially a mixture of minute amounts of epsom salt, calcium, iron, manganese, ammonia, carbonate, bicarbonate, sulfate, chloride and sulfur, with traces of iodides, bromides and possibly of copper, zinc and lithium. The article included the summary of this case by the Department's solicitor, Judge Vincent M. Miles, in which he said, in part, that although the name "Tru-Science" also was used by this Kansas City outfit it did not seem necessary to include it in the fraud order against the Natur-Food Company. Not long afterward, however, the Post Office discovered that the swindle was still being promoted by George Keyes assisted by Thelma Randall, the daughter of his original partner, and that they were now operating under the names Tru-Science, Natur-Tabs Company and Wilbur Hanson, North Kansas City, Mo. On May 23, 1941 the Post Office extended the earlier fraud orders to cover these last three names.

The Health Educational Clinic, R. L. Fraser, The Clinic of Preparedness and Mildred Hagaman.—From McCrory, Ark., Robert Lee Fraser, M.D., operated a mail-order business under the high sounding title, "The Health Educational Clinic" and sold something with the equally impressive name, "Heavy Vitamins." The Post Office Department charged that he promoted this nostrum under false and fraudulent pretenses, representations and promises to the effect that when used as directed it would cure, overcome, remove the cause of, and prevent the recurrence of cancer, colitis, eczema, athlete's foot, asthma, lumbago, pyorrhea, diabetes, pneumonia, prostate and bladder disorders, tuberculosis, chronic appendicitis, venereal diseases and some other things, regardless of the cause or severity of any of these conditions! And what was this cure-all? According to a government chemist who analyzed it, Heavy Vitamins contained 9.952 per cent by weight of sulfuric acid and 0.005 grain per hundred cubic centimeters of mineral matter, the remainder being water. The chemist further testified that he found no organic substances in the preparation. Expert medical evidence produced at the hearing showed that a solution having no organic substances could not contain vitamins, hormones or the amino-acids which Fraser claimed were present in Heavy Vitamins, in spite of his testimony that the product contained all the foods necessary to sustain life, including twenty-two amino-acids and a food for every gland in the body. Further, it was reported that Fraser's testimony admitted that he had never personally examined any of the patients whose records he submitted to determine whether or not the alleged improvements in their condition were actual, but that he had merely accepted their statements as being correct. As his various claims and representations were found to be unsubstantiated by scientific evidence, the Post Office Department issued a fraud order on June 23, 1941 against the Health Educational Clinic, Dr. R. L. Fraser as manager and founder and the officers and agents of his concern. Not long afterward the Post Office discovered that Fraser had resumed his enterprise and was operating not only under his own name and that of the Health Educational Clinic, but also under two new trade styles, the Clinic of Preparedness and Mildred Hagaman, Secretary. As a precaution, however, he was sending his nostrum out through private express companies and explaining in his letters to customers that he could no longer *mail* Heavy Vitamins but would have to ship the stuff by express, "due to 5th Column interference through the postoffice department." The second fraud order, issued against the two new trade styles that Fraser was using, was issued Oct. 28, 1941.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

BOARDS OF MEDICAL EXAMINERS
BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, March 28, page 1159.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Parts I and II.* Various centers, June 22-24. *Part III.* Various centers, June or July. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOGY: *Oral. Groups A and B.* Cleveland, Jan. 14-15, 1943. Final date for filing application is Dec. 7. *Written.* Various centers, Nov. 16. Final date for filing application is Oct. 5. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* St. Paul, April, in advance of the meeting of the American College of Physicians and June, Philadelphia, in advance of the meeting of the American Medical Association. Application should be on file 6 weeks in advance of the date of oral examination. *Written.* Oct. 19. Final date for filing application is Sept. 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* New York, May 12-13. Sec., Dr. R. Glen Spurling, 404 Brown Bldg., Louisville, Ky.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* Baltimore, June 6 and Philadelphia, June 8. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Oral and Written.* Chicago, Jan. 9-10. Final date for filing application is Nov. 1. Sec., Dr. Guy A. Caldwell, 3503 Prytania St., New Orleans.

AMERICAN BOARD OF PEDIATRICS: *Written.* Locally, Sept. 18. *Oral.* Chicago, Nov. 2-3. Final date for filing application is July 1. Sec., Dr. C. A. Aldrich, 707 Fullerton Ave., Chicago.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, December. Final date for filing application is Oct. 1. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Contracts: Validity of Contract Restricting Right to Practice Optometry.—The plaintiff operated a number of jewelry stores throughout the state of New York and employed the defendant, a licensed optometrist, in the optical department of one of those stores. The defendant's contract of employment, executed in February 1939, contained two specific covenants. The first provided, in substance, that during his employment, or for one year thereafter, the defendant would not engage in any business that competed with the plaintiff within a radius of 10 miles of any city, town or village in which the plaintiff operated a store. The second restrained the defendant, during the same period of time, from divulging any of the plaintiff's trade secrets or soliciting the patronage of any of the plaintiff's customers. On Jan. 11, 1940 the defendant resigned from the plaintiff's employ, rather than be transferred to another town, and on Feb. 1, 1940 he opened his own office for the practice of optometry in the town in which he had been employed by the plaintiff. The plaintiff therefore filed a suit in the supreme court, Broome County, N. Y., to enjoin the defendant from breaching the aforementioned covenants.

Contracts and agreements of this character, said the supreme court, have been enforced when they are not unduly harsh, unreasonable or inequitable. The court, however, held that the contract in this case was much broader in scope than was necessary to protect the plaintiff's interests. The contract in question assured the defendant neither a definite tenure of employment nor a definite wage. He could have been discharged the next day or his wages could have been substantially reduced. The plaintiff already operated stores in many places in the state and might in the future extend such activities to every sizable community. The result of this would be completely to eliminate the defendant from practicing optometry in the state of New York for one full year. Such a result, concluded the court, was inequitable and would be disastrous to a young professional man. The court further held, however, that the provi-

sions of the second restrictive covenant were fair and should be enforced. It would be most unreasonable, the court said, to allow the defendant to steal the plaintiff's customers through a knowledge of their identity gained by him as an employee. The court therefore held in effect that the defendant could maintain his private office but that he could not build up his practice by taking advantage of the acquaintanceships made during his prior employment by the plaintiff.—*Rudolph Bros., Inc. v. Greulick, 21 N. Y. S. (2d) 971 (N. Y. 1940).*

Poisoning: Lead Poisoning of Infant Attributed to Metallic Breast Shields.—The infant plaintiff was born in a New Jersey hospital on June 6, 1936. His mother obtained and used metallic lead nipple shields. Accompanying the shields was a circular describing the history of their development and stating, in part:

> For the prevention and cure of sore nipples these shields should be applied as soon after delivery as possible, and in using them the only attention required is to wipe the nipple previously to nursing and apply the shield again immediately afterwards. *They are in no way likely to be injurious to the infant.*

The mother said that she used the shields until sometime in January 1937, always being careful thoroughly to wipe each breast with a boric acid solution before feeding the infant. In January the infant became violently ill and was removed to a hospital, where his condition was diagnosed as lead poisoning. In a subsequent suit for damages brought on behalf of the infant against the vendor of the shields, the complaint was dismissed by the supreme court, trial term, Kings County, New York.

The plaintiff argued that lead from the metallic shields was deposited in the fissures of the mother's sore breasts and that the ingestion of this lead by the infant over a period of months caused the infant's illness. The contention was that the nipple shields were not only inherently dangerous but were marketed without proper warning or instructions. The supreme court admitted that a person marketing inherently dangerous products must give fair and adequate warning or instructions to the using public. The evidence showed, however, that many thousands of these shields had been used, both in England and in the United States, for more than ninety years, but that in all that time only once had any member of the medical profession questioned the safety or efficiency of their use. That one occasion was in an article published in THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, May 15, 1926, in which reference was made to 2 cases. One of those cases, the court said, was hearsay and the other showed that the mother had been negligent in washing her nipples. In fact the article stated:

> Lead poisoning in nursing infants is extremely rare. . . . One cannot be certain that the nursing infants may not also have sucked lead from the skin or hair of the mothers, or carried it to their mouths on their hands.
>
> . . . we have not found the use of lead nipple shields by nursing mothers previously demonstrated as a source of lead poisoning in infancy.

The article also enumerated other sources of lead poisoning in infants of nursing age as glass nursing bottles containing lead; nursing bottle stoppers, both of metallic lead and of lead-containing rubber and lead frames in which nursing bottles are held; lead powders used by mothers as cosmetics, and inhalation of lead dust, lead paint from a doll and clothing material impregnated with lead. The court added that many persons are allergic to conditions which do not affect the normal individual and that, from the evidence, there was no way of determining whether or not the infant in this case was the subject of a peculiar hypersensitivity to the almost insignificant lead deposits on the mother's breasts.

The plaintiff was required to prove, first, that the injury resulted from lead ingested, even though the mother followed the directions accompanying the shields; second, that the shields were inherently dangerous and poisonous; and, third, that the defendant was negligent in marketing such dangerous and poisonous appliances. The court stated the general principle applicable to the sale of inherently dangerous products: "There must be knowledge of a danger, not merely possible, but probable." The evidence in this case, said the court, showed that the metallic shields had been used by many thousands of persons and over a long period of time without resultant harm. Neither the manufacturer nor the marketer had any knowledge or indication that the product was in any sense dangerous. Since the defendant knew of no dangers against which the public should have been warned, it was not negligent in putting such product on the market in the manner in which it did. A manufacturer, concluded the court, may not be charged with negligence where some unusual result occurs that cannot reasonably be foreseen and is not within the compass of reasonable probability. The court therefore held that the evidence failed to sustain the allegations of the complaint. Complaint dismissed and judgment for the defendant.—*Cleary v. John M. Maris Co., 19 N. Y. S. (2d) 38 (N. Y., 1940).*

Malpractice: Liability of Hospital for Negligent Acts of Nurse During Operation.—The patient submitted to a cystoscopy in the defendant hospital, a private noncharitable institution. When the physician was ready to perform the operation, he asked a nurse, employed by the defendant hospital and in charge of the operating room, for a 5 per cent solution of cocaine and informed her that there was a 10 per cent solution in the cabinet. The nurse prepared a solution and gave it to the defendant physician, who injected it into the patient's urethra preliminary to passing a catheter. The physician immediately detected an unexpected reaction, and an examination of the bottle from which the solution was taken disclosed that it had contained sodium hydroxide instead of cocaine. Both solutions were colorless and odorless. As a result of the injection of sodium hydroxide, the patient suffered serious burns which developed into strictures. The patient died fifteen months later from other causes, but his executor filed suit in the supreme court, Nassau County, N. Y., against both the physician and the hospital for damages allegedly caused by the injection. The jury returned a verdict in favor of the defendant physician and against the defendant hospital. The trial court, however, granted the hospital's motion to set aside the verdict and dismiss the plaintiff's complaint.

The general competence of the nurse was not questioned; nor were there any suggestions that the hospital had been negligent in either hiring her or retaining her in its employ. The defendant hospital contended, however, that it was not responsible for the negligence of its nurse in the treatment of patients. A hospital, said the court, whether charitable or private, is immune from liability for the negligence of its doctors or nurses with respect to any matter relating to the patient's medical care and attention. In *Schloendorff* v. *Society of New York Hospital,* 211 N. Y. 125, 105 N. E. 92, the plaintiff sought to recover damages from the defendant hospital because of an unauthorized operation performed by members of the hospital staff. The court held that, in the performance of an operation, the physicians were pursuing an independent calling and were not acting as agents of the hospital. The court then added "It is true, I think, of nurses, as of physicians, that, in treating a patient, they are not acting as the servants of the hospital." In the instant case the evidence clearly showed that at the time of her negligence the nurse was assisting the physician in the operating room and attempting to follow his directions and was not acting in the discharge of administrative duties to the hospital. Relying on the Schloendorff case, the supreme court said that acts of preparation immediately preceding an operation are necessary to its successful performance and are really part of the operation itself. They are not different in that respect from the administration of the ether, the court continued, and whatever the nurse does in those preliminary stages is done, not as the servant of the hospital, but in the course of the treatment of the patient, as the delegate of the surgeon to whose orders she is subject. Accordingly the motion of the defendant hospital to dismiss the plaintiff's complaint was granted. This judgment was subsequently affirmed by the supreme court, appellate division, second department.—*Steinert v. The Brunswick Home, Inc., et al., 16 N. Y. S. (2d) 83 (N. Y., 1939); 20 N. Y. S. (2d) 459 (N. Y., 1940).*

Society Proceedings

COMING MEETINGS

Alabama, Medical Association of the State of, Montgomery, Apr. 21-23. Dr. D. L. Cannon, 519 Dexter Avenue, Montgomery, Secretary.

American Association of Genito-Urinary Surgeons, Hershey, Pa., May 27-29. Dr. Charles C. Higgins, 2020 East 93d St., Cleveland, Secretary.

American Association of Industrial Physicians and Surgeons, Cincinnati, Apr. 13-17. Dr. Edward C. Holmblad, 28 East Jackson Blvd., Chicago, Managing Director.

American Association of the History of Medicine, Atlantic City, N. J., May 3-5. Dr. Henry E. Sigerist, 1900 East Monument St., Baltimore, Secretary.

American Association on Mental Deficiency, Boston, May 13-16. Dr. Neil A. Dayton, 100 Nashua St., Boston, Secretary.

American College of Physicians, St. Paul, Apr. 20-24. Mr. E. R. Loveland, 4200 Pine St., Philadelphia, Executive Secretary.

American Federation for Clinical Research, Minneapolis, Apr. 20-21. Dr. Thomas M. Durant, 3401 North Broad St., Philadelphia, Secretary.

American Laryngological Association, Atlantic City, N. J., May 25-27. Dr. Charles J. Imperatori, 108 East 38th St., New York, Secretary.

American Otological Society, Atlantic City, N. J., May 28-29. Dr. Isidore Friesner, 101 East 73d St., New York, Secretary.

American Pediatric Society, Sky Top, Pa., Apr. 30-May 2. Dr. Hugh McCulloch, 325 North Euclid Ave., St. Louis, Secretary.

American Psychiatric Association, Boston, May 18-22. Dr. Winfred Overholser, St. Elizabeths Hospital, Washington, D. C., Secretary.

American Society for Clinical Investigation, Atlantic City, N. J., May 4. Dr. Eugene M. Landis, University of Virginia Hospital, Charlottesville, Va., Secretary.

American Surgical Association, New Orleans, Apr. 6-8. Dr. Charles G. Mixter, 319 Longwood Ave., Boston, Secretary.

Arizona State Medical Association, Prescott, May 25-30. Dr. W. Warner Watkins, 15 East Monroe St., Phoenix, Secretary.

Arkansas Medical Society, Hot Springs National Park, Apr. 27-29. Dr. W. R. Brooksher, 602 Garrison Ave., Fort Smith, Secretary.

Association of American Physicians, Atlantic City, May 5-6. Dr. Hugh J. Morgan, Vanderbilt University Hospital, Nashville, Tenn., Secretary.

California Medical Association, Del Monte, May 4-7. Dr. George H. Kress, 450 Sutter St., San Francisco, Secretary.

Florida Medical Association, Palm Beach, Apr. 13-15. Dr. Shaler Richardson, 111 West Adams St., Jacksonville, Secretary.

Georgia, Medical Association of, Augusta, Apr. 28-May 1. Dr. E. D. Shanks, 478 Peachtree St. N.E., Atlanta, Secretary.

Illinois State Medical Society, Springfield, May 19-21. Dr. Harold M. Camp, 224 South Main St., Monmouth, Secretary.

Iowa State Medical Society, Des Moines, Apr. 15-17. Dr. Robert L. Parker, 3510 Sixth Ave., Des Moines, Secretary.

Kansas Medical Society, Wichita, May 11-14. Mr. C. G. Munns, 112 West Sixth St., Topeka, Executive Secretary.

Louisiana State Medical Society, New Orleans, Apr. 27-29. Dr. P. T. Talbot, 1430 Tulane Ave., New Orleans, Secretary.

Maryland, Medical and Chirurgical Faculty of, Baltimore, Apr. 28-30. Dr. Richard T. Shackelford, 1211 Cathedral St., Baltimore, Secretary.

Massachusetts Medical Society, Boston, May 26-27. Dr. Michael A. Tighe, 8 Fenway, Boston, Secretary.

Medical Library Association, New Orleans, May 7-9. Miss Anna C. Holt, 25 Shattuck St., Boston, Secretary.

Mississippi State Medical Association, Jackson, May 12-14. Dr. T. M. Dye, P. O. Box 295, Clarksdale, Secretary.

Missouri State Medical Association, Kansas City, Apr. 27-29. Mr. E. H. Bartelsmeyer, 634 North Grand Blvd., St. Louis, Executive Secretary.

National Tuberculosis Association, Philadelphia, May 6-9. Dr. Charles J. Hatfield, 1790 Broadway, New York, Secretary.

Nebraska State Medical Association, Omaha, May 4-7. Dr. R. B. Adams, 416 Federal Securities Bldg., Lincoln, Secretary.

New Hampshire Medical Society, Manchester, May 12-13. Dr. Carleton R. Metcalf, 5 South State St., Concord, Secretary.

New Jersey, Medical Society of, Atlantic City, Apr. 21-23. Dr. Alfred Stahl, 55 Lincoln Park, Newark, Secretary.

New York, Medical Society of the State of, New York, Apr. 27-30. Dr. Peter Irving, 292 Madison Ave., New York, Secretary.

New York State Association of Public Health Laboratories, Cooperstown, May 18. Miss Mary B. Kirkbride, New Scotland Ave., Albany, Secretary.

North Carolina, Medical Society of the State of, Charlotte, May 11-13. Dr. Roscoe D. McMillan, P. O. Box 232, Red Springs, Secretary.

North Dakota State Medical Association, Jamestown, May 18-20. Dr. L. W. Larson, 221 Fifth St., Bismarck, Secretary.

Ohio State Medical Association, Columbus, Apr. 28-30. Mr. C. S. Nelson, 79 East State St., Columbus, Executive Secretary.

Oklahoma State Medical Association, Tulsa, April 22-24. Mr. R. H. Graham, 210 Plaza Court Bldg., Oklahoma City, Executive Secretary.

Pacific Coast Oto-Ophthalmological Society, Portland, Ore., May 11-14. Dr. C. Allen Dickey, 450 Sutter St., San Francisco, Secretary.

South Carolina Medical Association, Myrtle Beach, May 19-21. Dr. Julian P. Price, 105 West Cheves St., Florence, Secretary.

South Dakota State Medical Association, Sioux Falls, May 13-15. Dr. Clarence E. Sherwood, 107½ Egan Avenue South, Madison, Secretary.

Tennessee State Medical Association, Memphis, Apr. 14-16. Dr. H. H. Shoulders, 706 Church St., Nashville, Secretary.

Texas, State Medical Association of, Houston, May 11-14. Dr. Holman Taylor, 1404 West El Paso St., Fort Worth, Secretary.

CENTRAL SOCIETY FOR CLINICAL RESEARCH

Fourteenth Annual Meeting, Held in Chicago, Nov. 7 and 8, 1941

The President, DR. LAWRENCE D. THOMPSON, St. Louis, in the Chair

(Continued from page 1162)

Studies in Immunity to Influenza Virus and Hemolytic Streptococcus Infections

DRS. CHARLES A. DOAN, ORAM C. WOOLPERT, CESAR MERINO, JOHN SCHWAB, MARION BEARD and S. SASLAW, Columbus, Ohio: Schwab, Blubaugh and Woolpert in preliminary experiments, employing mice, observed a shorter survival period and a higher mortality rate in animals inoculated intranasally with mixtures of Streptococcus hemolyticus group C (Lancefield) and influenza virus A than in those receiving either agent alone. Recently Andrews and Glover have demonstrated conclusively the aerial transmission of a combined streptococcic-influenzal infection in ferrets.

That more detailed analyses of the humoral and cellular reactions occurring under such conditions might be made, exploratory studies were begun some two years ago on Macaca mulatta monkeys. It has been found that an intranasal instillation of 10,000 mouse minimum lethal doses of influenza virus A is followed promptly by the appearance of a striking granulopenic leukopenia and that within eight to twelve days virus neutralizing antibodies may be demonstrated in the blood serum coincident with the reestablishment of the preinfection white cell equilibrium. Fever, anemia, anorexia and positive blood cultures were not observed, and no fatalities occurred in cases of this mild, uncomplicated infection.

Parallel intranasal inoculations of 750,000,000 hemolytic streptococci of group C produced in normal monkeys an immediate characteristic polymorphonuclear leukocytosis, the white cells numbering 30,000 to 50,000 per cubic millimeter, fever, anorexia, gradual weight loss and progressive hemolytic anemia with reticulocytosis. Cultures from the throat remained positive for these organisms for variable periods. The opsonocytophagic index, precipitin and antistreptolysin titers remained unchanged. The cellular defenses, as reflected in the fluctuating granulocytosis, gradually prevailed, and coincident with the reestablishment of the preinfection equilibrium in the white cells the hemolytic streptococci disappeared from the throat and the temperature became normal. Most significant of all, the anemia, which had been progressive up to this point, was reversed, and a spontaneous return to normal of the red cell and hemoglobin values promptly followed. All normal monkeys under optimum dietary conditions survived this initial infection with hemolytic streptococci.

As might be anticipated, an occasional animal continued to harbor hemolytic streptococci in the throat. In such animals spontaneous clinical exacerbations occurred with the development of albuminuria, hematuria, edema and hypertension, with histologic evidence of renal pathologic conditions post mortem. In recovered monkeys reinoculation with the organism was accomplished three to five months after the original infection. In sharp contrast to the original reactions, no leukocytosis, and little or no fever or other constitutional manifestations of disease developed, but the opsonocytophagic index rose sharply within twenty-four hours, suggesting a greater individual acquired polymorphonuclear efficiency in dealing with the invaders.

In other experiments the initial influenza virus infection was followed in four days and seventeen days respectively by superimposed hemolytic streptococcus infection. Usually the charac-

teristic polymorphonuclear leukocytosis was observed in monkeys which had received the virus only four days previously, and survival was the rule.

In the others, however, the leukocytosis was completely inhibited, and in 1 animal (monkey 3) death followed within thirty-two days of the original virus infection and on the fifteenth day after the superimposed streptococcus inoculation, with generalized sepsis, as proved by repeated blood cultures and cultures of all organs post mortem.

When hemolytic streptococcus infection was followed by a superimposed virus inoculation at the same two arbitrary time intervals, the virus invasion, after the four day interval, was reflected either by transitory leukopenia (lasting twenty-four hours) or by delayed granulocytopenia (lasting ten to fifteen days) and the neutralizing antibodies were demonstrable as in the uncomplicated influenzal infections. When a seventeen day interval was permitted to elapse, usually all evidence of the streptococcic infection had disappeared and the influenzal reaction occurred with characteristic leukopenia, followed by appearance of neutralizing antibodies in the time relationships already described.

When influenza virus and hemolytic streptococci were instilled simultaneously into the nasal passages of normal monkeys, immediate leukocytosis developed and subsequently leukopenia suggestive of a delayed virus effect.

The relative mildness of the clinical manifestations, associated with the distinctive humoral and cellular reactions, which reflect invasion of mucous membrane by the agents employed, make the normal healthy, well nourished monkey an ideal medium for this type of study. Preliminary investigations with various deficient diets already indicate a materially altered resistance in terms of the factors here analyzed, with a corresponding alteration of clinical morbidity and mortality.

DISCUSSION

DR. M. A. BLANKENHORN, Cincinnati: I should like to ask Dr. Doan whether he has been able by the combination of these things to cause a definite pathologic picture in the lungs. In particular, has he been able to produce the pathologic picture seen in the lungs of patients who died in the epidemic of influenza of 1918 and thereabouts?

DR. C. A. DOAN, Columbus, Ohio: There has been 1 spontaneous death in this particular series. At autopsy the monkey showed pathologic changes in the lung suggestive of those seen in human bronchopneumonia. We have been interested in following the lung fields, both clinically and roentgenographically, in the surviving monkeys, but there has been no evidence significant of gross pathologic changes in the lung. This does not mean that there might not be microscopic histologic changes; that remains to be seen. Because of the scarcity of monkeys we have not yet deliberately killed animals at various stages during the humoral and cellular reactions for tissue studies. Such observations are currently being made. The monkey seems to be more resistant to clinical influenza of type A than the human being and is much more resistant than ferrets and mice. Judging solely from the clinical manifestations, there is no evidence for invasion by the virus at all. It is only by following the peripheral blood cell and blood serologic changes from day to day that one may obtain indirect evidence of invasion. There have been negative reports heretofore, based on clinical data alone, of infection by the influenza virus in monkeys.

The Coagulase Test for Staphylococci

DR. WESLEY W. SPINK and JEAN JERMSTA, B.A., Minneapolis: Several in vitro tests for determining pathogenicity of staphylococci have been developed in the past. The simplest and most satisfactory clinical method is the coagulase test. An intensive study of seventy strains of staphylococci in the past three years reveals that the coagulase positive strains resist the bactericidal action of human blood. This correlation is remarkably constant. Our studies indicate that serious infections and invasion of the blood stream are due to coagulase positive strains with important exceptions that will be discussed. In 2 instances invasion of the blood stream by coagulase negative Staphylococcus albus strains resulted in death because of the localization of the organisms on the heart valves and the establishment of subacute bacterial endocarditis.

Thermal Effect of Renal Extracts on Guinea Pigs

JOSEPH ZICHIS, PH.D., and DRS. MAURICE WALD, MORRIS E. THOMAS and M. HERBERT BARKER, Chicago: In the preparation and study of renal tissue extracts (Page and his co-workers) a rapid method of assay is urgently needed. When young guinea pigs weighing from 140 to 200 Gm. are inoculated intraperitoneally with 1 to 2 cc. of a clinically active renal extract severe hypothermia results. The hypothermic reaction appears in one to two hours, the greatest temperature fall, of 4 to 10 degrees Fahrenheit, being reached in four to eight hours, and return to normal occurs in twenty-four to thirty-six hours. In addition some of the animals have shown a shocklike reaction. Ten per cent die within twenty-four hours. Inactivated renal extracts, serums and other tissue extracts fail to show this characteristic hypothermic reaction.

In dogs with experimental hypertension, produced by wrapping the kidneys in silk, who present the picture of the malignant stage (blood pressure over 200 mm., detached retinas, listlessness, toxicity and inability to eat or drink), the administration of active extracts greatly improves the general condition. The appetite returns, the dogs move about their cages and the retina shows varying degrees of improvement, with and occasionally without notable falls of the blood pressure.

Patients exhibiting the signs and symptoms of so-called malignant hypertension treated with active renal extracts often show more improvement in their symptoms than fall in the blood pressure. The order of improvement is generally that the headaches disappear, there is a general feeling of well-being, the gallop rhythm of the heart subsides and the retinas clear of hemorrhages, exudate and papilledema. It should be stated that the average fall in systolic blood pressure ranges from 30 to 50 mm. of mercury and the diastolic 15 to 30 mm. Patients with benign or essential hypertension show a more decided fall in blood pressure associated with the disappearance of the headaches, vertigo, dyspnea, constipation and fatigability.

The hypothermic reaction has been correlated with the symptomatic improvement and a decrease in the blood pressure in both experimental animals and patients. Extracts which have produced a sharp drop in temperature in guinea pigs have regularly shown moderate to considerable clinical effect. Extracts which have produced no or slight response of the temperature have shown little or no therapeutic benefit. It is hoped that this or some similar simple test can be found to facilitate the purifying of the hypotensive factor in renal tissue extracts.

Effect on Cardiac Output of Renal Extracts

DRS. ROBERT D. TAYLOR and IRVINE H. PAGE, Indianapolis: Ballistocardiographic observations of the cardiac output were made on 15 hypertensive patients before and after treatment with extracts of kidneys ("angiotonin inhibitor") and on normal human subjects before and after administration of angiotonin, tyramine and methylguanidine sulfate.

When arterial pressure was reduced in hypertensive patients the cardiac output increased roughly 15 to 20 per cent. When extract was withdrawn and the arterial pressure rose the cardiac output decreased to its former level.

Hypertension induced in normal persons by tyramine and methylguanidine was accompanied by highly unpleasant symptoms, whereas that from angiotonin was not. The stroke volume was increased with tyramine, but coincident bradycardia reduced cardiac output. Methylguanidine produced slight bradycardia, reduced stroke volume and cardiac output. Angiotonin, on the other hand, produced little change in pulse rate and considerable reduction in stroke volume and cardiac output.

The results add evidence in favor of the view that the angiotonin-angiotonin inhibitor system plays a part in the genesis of human arterial hypertension.

The Use of Kidney Extract in Controlling Experimental Renal Hypertension and Essential Hypertension

DRS. FRANCIS D. MURPHY, JOHN GRILL, G. P. LANGENFELD, L. J. KURTEN and V. G. GUENTHER, Milwaukee: A kidney extract has been prepared from pork kidneys according to a method described by Page. It has been used to treat 11 patients with essential hypertension and rats with experimental renal hypertension. The results obtained were as follows: Seven of the 11 patients responded satisfactorily, 2 were resistant and 2 were symptomatically improved without a corresponding drop in blood pressure. All the patients had either premalignant or malignant forms of essential hypertension.

The unfavorable features have been the local and the general reactions. The local type, although painful, is not dangerous. There are two kinds of general reactions: the anaphylactic-like type, and the more dangerous kind that is associated with a sharp fall in blood pressure and peripheral vascular collapse.

Rats made hypertensive by Page's method were used for control of the extract before it was injected into patients.

DISCUSSION ON RENAL EXTRACTS

DR. EMMET B. BAY, Chicago: I should like to ask Dr. Taylor how the calculations on cardiac output from ballistocardiographic records are made with special reference to the underlying formula to which Starr has referred, i. e. that $f = m\ a$, an old-time physical equation. I can see how m in the equation could represent output if it can be separated from a, which represents acceleration. In the presence of a lowered diastolic blood pressure the emptying time of the ventricle might be decreased, and would not this as well as the increased output increase the a of acceleration? Is this taken into account in the calculations? These records probably show improvement in circulatory dynamics, whether or not one can say anything more than that.

DR. GEORGE E. WAKERLIN, Chicago: It is highly desirable to have a shorter method of assaying antipressor extracts than the present one involving the use of dogs, rabbits or rats with renal hypertension. Perhaps the method reported by Dr. Zichis and his co-workers is the one investigators are looking for. This procedure may be similar in principle to the frog method for digitalis. Digitalis assay in the frog, of course, involves the production of a toxic effect, which is essentially an exaggerated therapeutic response, by large doses of the drug. Obviously, more work is necessary before the method proposed can be finally evaluated. The finding of Drs. Taylor and Page that angiotonin decreased the cardiac output in normotensive human beings is most interesting. In view of the well known fact that the cardiac output is within normal limits in essential hypertension, how can the action of angiotonin on the cardiac output in human normotension be adduced as evidence for a pathogenic role for angiotonin in essential hypertension? Did Dr. Murphy and his co-workers control the possible nonspecific effect of the kidney extract in their experiments by treating a group of hypertensive patients with a similarly prepared extract of hog tissue other than the kidney?

DR. HENRY N. HARKINS, Detroit: I was interested in the side effects of one of the extracts mentioned by Dr. Zichis and Dr. Langenfeld, namely the local reactions, shock and death after injections in guinea pigs. Was the peritoneal fluid of the guinea pigs that died increased in amount, and if so was it a protein-like fluid or merely a watery transudate? Some years ago the late Dr. Andrews and I showed that a number of substances, among them bile and bile salts, if injected into the peritoneal cavity in large amounts would cause a local weeping of plasma-like fluid with resultant secondary shock. The shock described by Dr. Zichis might be such a local reaction or it might be caused by the general effects of the fluid after absorption.

DR. FRANCIS D. MURPHY, Milwaukee: As to the cases reported by Dr. Langenfeld, I believe it should be emphasized once more that the patients had had hypertension for a long time before we used the kidney extract; so I do not believe we were fooled in our interpretation by the old post hoc ergo propter hoc argument. In our cases malignant hypertension failed to respond satisfactorily to treatment, while Dr. Page and his associates have reported favorable results in some of their cases of malignant hypertension. This difference may be explained by the fact that so-called malignant hypertension may occur in some patients who have had long-standing hypertension and well developed renal arteriosclerosis, while in others the malignant syndrome may be engrafted on a fairly normal kidney to begin with. It seems to me that there would be a distinct difference as far as treatment with renal extract is concerned in these two sets of cases. I do not wish to offer these cases as proof that kidney extract is a cure or that it solves the problem of therapeutics in essential hypertension. After using this extract, crude as it is, for about a year, we obtained satisfactory results in about 75 per cent of the cases. When a purer extract is produced a higher percentage of favorable responses is anticipated.

DR. LOUIS N. KATZ, Chicago: The question has been raised whether the ballistocardiograph is a suitable recorder of cardiac output. When Dr. Starr first described this method it did not appear to be sufficiently accurate, but more recent work has convinced me that it can give information of the output of the heart by the methods suggested by Dr. Starr. However, it should not be used for individual cases but rather for a statistical handling of a large series. With regard to the report by Dr. Murphy and his collaborators, I should like to point out that at present the extract of the kidney which has been employed requires large quantities of kidney. It is therefore not practical. Why cannot something be done to improve the manner of extracting so that a better yield can be obtained? Only when this is accomplished will the method have possibilities for widespread clinical use.

DR. PAUL STARR, Chicago: The authors conclude that the extract which lowers the blood pressure is one that benefits the patient. Is it necessarily true that lowering the blood pressure will lengthen the life of the patient?

DR. MORRIS THOMAS, Chicago: In our work with the kidney extract we found considerable symptomatic improvement. In most of the cases there has been a fall in the blood pressure. That is true in cases of malignant hypertension. The indications of improvement have been the disappearance of headaches, improvement in the general feeling of well-being, disappearance of gallop rhythm and clearing of the hemorrhagic exudates previously present in the eyes. There have been no remissions unless the extract was withdrawn. Recently we have been working with benign or simple hypertension, and we have noted in the patients a much greater fall in blood pressure. In 1 with severe essential hypertension the blood pressure was reduced to 145 systolic and 90 diastolic, but with withdrawal of the extract the pressure rose in a few days to 206 to 220 systolic and 120 to 140 diastolic.

DR. IRVINE H. PAGE, Indianapolis: All the kidney extracts which have been employed are crude. The question to be determined is whether there is an active depressor substance in them. With regard to Dr. Starr's question, it has long been thought on the basis of a teleologic explanation that elevation of the blood pressure is a desirable thing. Perhaps it is under certain circumstances, but on the whole the evidence points strongly the other way. We became convinced that the blood pressure could be lowered profoundly without the evidence of peripheral tissue anoxia. On the whole, clinical improvement seemed to follow reduction in blood pressure resulting from surgical operations, thiocyanate therapy or spontaneous reduction. Reduction of the arterial pressure in a hypertensive patient is desirable, not undesirable. It should be stressed especially that renal insufficiency does not occur even when the blood pressure falls sharply. The fear that it will occur appears unjustified. Measurement of the urea clearance following reduction of the blood pressure by a number of means showed beyond doubt that there was no gross over-all reduction in renal efficiency, but the interpretation of the urea clearance is complex;

hence it is necessary to resort to methods which give a more exact picture of the intrarenal hemodynamic changes. The insulin and diodrast clearances, as developed by Smith, Corcoran and Alving, will demonstrate such changes. The pathologic change which seems characteristic of the hypertension of most patients is constriction of the efferent glomerular arterioles with some reduction in total renal blood flow. The interesting fact demonstrated by Corcoran is that kidney extract causes relaxation of the efferent arterioles both in experimentally hypertensive animals and in human beings with hypertension along with a moderate increase in blood flow. As Corcoran and I have emphasized, the actual blood flow through the kidney is the result of two opposing factors: (1) the mean systemic arterial pressure working against (2) the effective resistance of the flow of blood through the kidney; thus if the resistance in the kidney is lowered at the same rate at which the mean arterial pressure is lowered there should be no increase in the renal blood flow. But such a direct proportionality is seldom seen with the administration of kidney extract, with the result that some increase occurs in blood flow along with relaxation of the efferent arterioles and fall in the systemic mean pressure. These observations suggest a certain degree of specificity in the kidney extract; I fully recognize the danger of using the term specificity. There is only scant evidence at present which suggests specificity, but, on the other hand, there is nothing against the notion that has so far been discovered which suggests that these extracts when properly prepared are not specific. The most obvious objection to the results obtained from study of the kidney is that the changes might be due to pyrogenic reactions. Pyrogens have been shown by Smith to cause an intrarenal hemodynamic change somewhat similar to that produced by kidney extract. Actually, thermal reactions have occurred in only a few patients. It seems unlikely that the changes could have been the result of pyrogenic reaction. Dr. Taylor has told you of the effect on the cardiac output. Again, this evidence might be taken to indicate the presence in kidney extract of a substance which is at least unusual in its action. The increase in the cardiac output which follows the reduction in the blood pressure is in some ways just the reverse of what one might anticipate. Perhaps one of the most dramatic effects of kidney extract is that on the eyegrounds. The reversal of the pathologic changes is often complete. Such reversal never occurs in malignant hypertension with the exception of hypertension concomitant with toxemia of pregnancy. I think one could say categorically that, whatever the nature of the kidney extract, its effect, direct or indirect, on the eyegrounds is remarkable. This emphasizes a point which I wish to make, namely that both Dr. Murphy's and our patients have for the most part had far advanced malignant hypertension. We have purposely chosen them because of the clarity with which objective evidences of the disease could be followed and because of the experimental nature of the work. We have not attempted to select patients who might give the best results, nor have we selected the extracts which give the best results. In general, it appears that when the renal function, as measured by diodrast Tm, is below 20 from the therapeutic point of view, giving kidney extract is hardly worth while. One could hardly expect to reverse the morbid process in kidneys so badly damaged, and keeping the patient alive is hardly more than a tour de force. I should like to point out that the preparation of these extracts is a question not so much of the difficult procedures involved as of the impurity of the end product and the poor yield. We are forced to work entirely empirically and up to recent months have had to depend on assay on hypertensive dogs and rats. Recently we have come to employ a test which determines the destruction of angiotonin and which we hope will facilitate assay greatly. Apparently the destruction of angiotonin and the lowering of blood pressure go hand in hand. I have had no personal experience with Dr. Zichis's test. I hope it will prove reliable because it would be an enormous time saver if it did. I do not consider the administration of kidney extract a practical treatment for hypertension at present. Whether it will become practical depends on future research, which is altogether unpredictable. Whether it proves practical or not it will open another avenue of approach to the difficult problem of hypertension. If the extracts contain substances with therapeutic activity more will be known about them in the course of time. But let me emphasize that if these are merely interesting substances which are found by more exacting testing to have no therapeutic effect then the search for them will have been a lot of fun; it is only when one enjoys one's research that it seems worth doing.

JOSEPH ZICHIS, PH.D., Chicago: I did not ordinarily observe the evidence of fluid concentration. After the guinea pig died all the material seemed to be absorbed, and we have not encountered peritonitis at all.

DR. ROBERT D. TAYLOR, Indianapolis: Dr. Katz helped me a good deal. The formula used was devised by Dr. Starr and published by him. He checked this method with the acetylene and ethyl iodide methods and found it to be within reasonable limits of accuracy in determining cardiac output. As for the decrease in cardiac output produced by angiotonin in normal persons, one must not forget that the experiments were with acute disease and the output cannot be compared with the state seen in chronic hypertension, which, as is well known, is usually normal. In hypertensive patients there is usually cardiac hypertrophy. In our patients we noted that those who had little or no cardiac hypertrophy had a low normal or a subnormal cardiac output, while those whose hearts were hypertrophied had an output in the high normal range. It may well be that the cardiac output in hypertension is maintained at a normal level by adaptative cardiac hypertrophy. In measuring cardiac output with the ballistocardiograph we noted some interesting changes in the tracings themselves. Over the past two years Dr. Isaac Starr has correlated various heart diseases with the tracings produced by the ballistocardiograph. Among the changes he has described is the "early M" complex usually seen in hypertension. This is produced by elevation of the normal H wave and shortening of the normal HI segment. These alterations combined with normal J and K waves produce a capital M. We have noted that angiotonin produces this in normal persons whereas tyramine and methylguanidine sulfate do not, and further that hypertensive patients treated with antipressor renal extracts produce tracings that compare to normal ones. Since both the ballistocardiographic and the renal hemodynamic changes of hypertension are mimicked by the action of angiotonin and, in patients with hypertension, reversed toward the normal by administration of antipressor renal extracts, a pathogenic role of angiotonin in hypertension seems not unlikely, and the specificity of these extracts is further confirmed.

DR. G. P. LANGENFELD, Milwaukee: The only question that has not been discussed is whether other tissue has been extracted or injected as a control. We have not used any other tissue in this way. The only one used has been kidney tissue.

The Localization of Human Bundle Branch Block

DRS. W. C. BUCHBINDER and FRANK NEUWELT, Chicago: The simultaneous registration of the arterial pulse wave (brachial) by the Hamilton manometer and the electrocardiogram was secured on 37 patients having intraventricular block with a QRS complex of 0.12 second or more. The time difference between the onset of mechanical ejection of the left ventricle and the electrical systole (QE interval) was determined for the 37 and for 20 patients without block who served as controls. The patients with intraventricular block were then separated into functional groups: (1) those having a normal QE interval and (2) those showing an interval prolonged by nearly 50 per cent. Each group shows distinctive electrocardiographic patterns. In the first, QRS_1 was chiefly down or an S wave was present; in the second, QRS_1 was up. The data presented are pertinent to localization of human bundle branch block lesions and are in accordance with the current views localizing the common type in the left bundle system and the uncommon or the one showing an S_1 in the right bundle system.

(To be continued)

Current Medical Literature

AMERICAN

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Titles marked with an asterisk (*) are abstracted below.

Alabama State Medical Assn. Journal, Montgomery

11:181-216 (Dec.) 1941

X-Ray Therapy: Indications in Everyday Practice. W. D. Anderson, Tuscaloosa.—p. 181.
Management of Esophageal Strictures. G. T. Johnson, Mobile.—p. 186.
Traumatic Rupture of Bladder and Urethra: Surgical Management. J. M. Townsend, Birmingham.—p. 188.
Vitamin Therapy in Relation to Dermatology. R. P. Lester, Mobile. —p. 190.
Pneumothorax in the Home. K. N. Joseph, Birmingham.—p. 197.
Modern Treatment of Sinal Disease. E. R. Nodine, Andalusia.—p. 199.

11:217-260 (Jan.) 1942

*Thymol Therapy in Tuberculosis: Preliminary Report. H. B. Searcy, R. McBurney, Tuscaloosa, and H. S. Rowe, Mount Vernon.—p. 217.
Pathologic Lesions in Macula and Area Centralis. K. B. Benkwith, Montgomery.—p. 221.
Management of Third Stage of Labor. T. B. Woods, Dothan.—p. 226.
Error and Delay in Diagnosis of Hydronephrosis. E. C. Coats, Florence. —p. 230.

Thymol in Tuberculosis.—Searcy and his co-workers administered 0.3 Gm. of thymol three times a day in the treatment of advanced pulmonary tuberculosis among 6 uncooperative patients. The thymol was given after each regular meal with a glass of whole milk to facilitate absorption. After seven weeks of therapy the patients had improved to such a degree that the daily dose was reduced to 0.3 Gm. given twice a day. During treatment there was no change of environment or of the dietary regimen. After nine weeks of treatment none of the patients had experienced any ill effects from the therapy. The authors realize that their clinical material is meager and that not enough time has elapsed to permit definite conclusions, but they believe that the improvement in their 6 patients is too uniform to be a coincidence. They suggest that the beneficial effect of thymol therapy in fungous disease warrants further study of the use of thymol, thymol combinations and derivatives in the mycobacterial diseases, i. e. tuberculosis and leprosy.

American Journal of Clinical Pathology, Baltimore

11:849-910 (Dec.) 1941

Behavior of Plasma Prothrombin in Pneumonia. L. M. Tocantins and W. A. Hause, Philadelphia.—p. 849.
Classification of Staphylococci. Emma S. Moss, Gretchen Vitter Squires and Anne C. Pitts, New Orleans.—p. 857.
Primary Carcinoma of Fallopian Tube. J. A. Tuta and W. A. Stuhr, Chicago.—p. 864.
*Basal Metabolic Rate in Low Grade Chronic Illness: Statistical Analysis of 166 Cases. M. H. Stiles, Philadelphia.—p. 871.
Relationship of "True Luschka Ducts," Adenomas and Aberrant Liver Tissue in Wall of Human Gallbladder. E. T. Thorsness, Denver.—p. 878.
Urolithiasis Medicamentosa Caused by Sulfadiazine. P. Gross, F. B. Cooper and M. L. Hagan, Pittsburgh.—p. 882.
Apocrine Sweat Gland Carcinoma of Vulva. J. R. McDonald, Rochester, Minn.—p. 890.

Basal Metabolism in Chronic Illness.—Stiles determined the basal metabolic rate of 166 persons with low grade chronic illnesses probably secondary to chronic infection. A low rate was the rule. The mean for the 166 persons was —8. Of these persons 83 per cent had a rate of 0 or below, and 43 per cent had a rate of —10 or less. Persons with moderately severe and severe symptoms of chronic illness had a significantly lower basal metabolic rate than did those with mild symptoms.

American Journal of Diseases of Children, Chicago

63:1-216 (Jan.) 1942

Cardiac Signs in Rheumatic Infection in Childhood. Rachel Ash, Philadelphia.—p. 1.
Salmonella Suipestifer Infections in Childhood. D. Gajzágó and O. Göttche, Budapest, Hungary.—p. 15.
Loneliness in Infants. H. Bakwin, New York.—p. 30.
Meningitis Due to Escherichia Coli: Report of Two Cases with Recovery Following Chemotherapy, Review of Literature and Report of Experimental Studies. G. S. Barrett, C. H. Rammelkamp and J. Worcester, Boston.—p. 41.
*Hypertension and Pyelonephritis of Children. G. C. Kimmel, Rochester, Minn.—p. 60.
Myatonia Congenita (Oppenheim) Accompanied by Congenital Intraspinal Tumor, Developmental Retardation and Malformation. F. H. Lewey, Philadelphia.—p. 76.
Dermatitis Due to "Antiseptic Oils." J. H. Lapin, New York.—p. 89.
Apparatus for Determination of Vital Capacity of Infants. H. M. Smith, S. McLanahan Jr., Baltimore, and W. C. Davison, Durham, N. C.—p. 92.
The Hyperactive Child. J. A. Russell, Washington, D. C.—p. 94.
Francis Home, M.D.: The Scottish Military Surgeon Who First Discovered Diphtheria. E. E. Hume, Carlisle Barracks, Pa.—p. 140.
Developmental Enamel Defects: Clinical Descriptions and Classification. B. G. Anderson, New Haven, Conn.—p. 154.

Hypertension and Pyelonephritis.—Kimmel reviewed the records of 510 children aged 2 months to 15 years who had pyogenic renal disease. Pathologic processes were demonstrated in 91 by urographic examination, at necropsy or at examination of a removed kidney. The group was further studied to determine in how many elevation of the blood pressure was present. For 33 of the children with unilateral renal lesions nephrectomy was performed, for 35 with unilateral renal lesions nephrectomy was not performed and in 23 the renal lesions were bilateral. Blood pressure was considered normal if it was less than 120 mm. of mercury systolic and 80 mm. diastolic, regardless of age. Of the first group of patients the blood pressure on admission in 1 was 138 systolic and 88 diastolic and four years later was 110 systolic and 60 diastolic; in 1 before operation it was 170 to 210 systolic and 140 to 166 diastolic and seven months after nephrectomy was 104 systolic and 74 diastolic. In 1 of the second group of patients on initial examination it was, respectively, 160 and 118 and 148 and 110 three years after an apparent cure after treatment with a ketogenic diet; in 1 on admission it was 148 and 90 and 120 and 80 two days after a nephrostomy on the left side; in 1 on admission it was 172 and 140 and nine months later after several dilations of the right ureter it dropped to 134 mm. systolic; and in 1 it was 200 and 170 soon after admission, and after a bilateral resection of the splanchnic nerve it dropped to 180 and 130. In 1 patient of the third group the blood pressure was 126 and 94 on admission, and five years later, after resection of the presacral nerve and resistance to methenamine and ammonium chloride, it was 142 and 98; in 1 on admission it was 142 and 104, and five years after a suprapubic cystostomy and a sphincterotomy it was 106 and 72; in 1 on admission it was 230 and 170, and after the patient had been five days in bed it was 160 and 120. The last patient died more than a year after dismissal. The age on admission of the 8 patients with hypertension varied from 7 to 14 years. In 3 of the 8, one atrophic kidney was present. In only 2 of the 8 was the level of urea in the blood elevated. Arteriolosclerosis was present in seventeen of the thirty-three pyelonephritic kidneys removed at operation. The view that renal ischemia may elevate the blood pressure in human beings seems to be suggested. Hypertension associated with chronic pyelonephritis in children apparently is not rare.

American Journal of Ophthalmology, Cincinnati

25:1-134 (Jan.) 1942

Microanatomy of Eye with Slit Lamp Microscope: II. Comparative Anatomy of Ciliary Body, Zonula and Related Structures in Mammalia. M. U. Troncoso, New York.—p. 1.
Aqueous Veins: Preliminary Note. K. W. Ascher, Cincinnati.—p. 31.
Early Diagnosis of Choroidal Melanomas. B. Rones, Washington, D. C. —p. 39.
Familial Incidence of Retinoblastoma with Genealogic Chart. H. F. Falls, Ann Arbor, Mich.—p. 42.
Conjunctivochalasis. W. L. Hughes, Hempstead, N. Y.—p. 48.
Ophthalmia Neonatorum: Etiology in Sixty-Two Consecutive Cases. S. H. McKee, Montreal, Canada.—p. 52.
Sulfathiazole in Treatment of Gonorrheal Eye Disease. C. R. Mullen, Philadelphia.—p. 59.
Clinical Photography, with Special Reference to Photography of Anterior Segment of Eye. D. W. Bogart, New York.—p. 62.

American Journal of Pathology, Ann Arbor, Mich.

18:1-168 (Jan.) 1942

Sclerosing Hemangiomas of Central Nervous System: Progressive Tissue Changes in Hemangioblastomas of Brain and in So-Called Angioblastic Meningiomas. O. T. Bailey and R. Ford, Boston.—p. 1.

Production of Cardiac and Renal Lesions in Rats by Diet Extremely Deficient in Potassium. R. H. Follis Jr., Elsa Orent-Keiles and E. V. McCollum, Baltimore.—p. 29.

Deposition of Calcium in Hearts and Kidneys of Rats in Relation to Age, Source of Calcium, Exercise and Diet. L. L. Barnes, Ithaca, N. Y.—p. 41.

Pathologic Changes in Nutritional Gastritis in Rats. B. N. Berg, New York.—p. 49.

Distribution of Intimal Atheromatous Lesions in Arteries of Rabbits on High Cholesterol Diets. S. L. Wilens, New York.—p. 63.

Pathology of Chastek Paralysis in Foxes: Counterpart of Wernicke's Hemorrhagic Polioencephalitis of Man. C. A. Evans, W. E. Carlson and R. G. Green, Minneapolis.—p. 79.

Intercapillary Glomerulosclerosis. R. C. Horn Jr. and H. Smetana, New York.—p. 93.

Glomerulonephritis in Partially Nephrectomized Rats: Relation to Administration of Sulfapyridine. P. Gross, F. B. Cooper and W. A. Morningstar, Pittsburgh.—p. 101.

*Interstitial Myocarditis Following Clinical and Experimental Use of Sulfonamide Drugs. A. J. French and C. V. Weller, Ann Arbor, Mich.—p. 109.

*Bronchiogenic Carcinoma in Association with Pulmonary Asbestosis: Report of Two Cases. H. B. Holleb and A. Angrist, Jamaica, N. Y.—p. 123.

Secondary Carcinoma in Cirrhosis of Liver. J. R. Lisa, C. Solomon and E. J. Gordon, New York.—p. 137.

Neuroblastoma, Ganglioneuroma and Fibroneuroma in Stillborn Fetus. Edith L. Potter and J. M. Parrish, Chicago.—p. 141.

Icterus of Adult Brain: Report of Case. Enid K. Rutledge and K. T. Neubuerger, Denver.—p. 153.

Bilateral Fusiform Aneurysms of Cervical Portion of Internal Carotid Arteries. J. G. Riddler, New Orleans.—p. 159.

Trypan Blue Vital Staining in Studies of Virus Lesions on Chorioallantoic Membranes. Jean V. Cooke and R. J. Blattner, St. Louis.—p. 163.

Myocarditis Following Chemotherapy.—French and Weller state that, during the last four years, interstitial myocarditis with eosinophilic cellular infiltration was occasionally encountered at necropsy at the University Hospital. Study revealed that medication during the terminal illness with one or more of the sulfonamide drugs was the only common factor. Survey of the necropsy material (1,706 patients) for 1937 to 1941 revealed that 283 patients had been given one or more of the drugs during the last few weeks of life. In 126 of these patients significant interstitial myocarditis was present. The age of the patients varied from 1 month to 87 years. The amount of the drug (administered over a few hours to several months before death) which apparently produced significant infiltration varied from 5 Gm. to more than 200 Gm. Interstitial myocarditis was not present in any patient who had not received chemotherapy for at least thirty days prior to death. No macroscopic changes attributable to the sulfonamide therapy were observed in the affected hearts. The microscopic features of the lesion included interstitial myocarditis, usually with a paravascular and sometimes also with a diffuse distribution of the cellular infiltrations. Both ventricles and auricles were widely involved. The looser auricular myocardium often exhibited a heavier paravascular infiltration than did the compact ventricular muscle. Some foci were likewise seen in the epicardium. The cellular infiltrations contained large mononuclear cells of clasmatocytic type and numerous cells with granular eosinophilic cytoplasm. Except for the acidophilic cytoplasm, some of the eosinophils resembled plasma cells. Eosinophilic infiltrations were occasionally observed in the liver, lungs and kidneys. In some instances the bone marrow, spleen and lymph nodes showed a relative increase in eosinophils. Similar eosinophilic interstitial myocarditis was produced in mice and rats receiving daily intraperitoneal injections of the sulfonamide drugs. The eosinophilic character of the infiltrations makes idiosyncrasy to the drugs seem likely. The lesions were not irreversible. Nevertheless, it is impossible to evaluate the effect that such a lesion might have on the heart of a person seriously ill from some other pathologic condition. Therefore, during therapy the efficiency of the cardiovascular system should be determined at frequent intervals. The authors stress the need of keeping patients who are receiving these drugs under the closest clinical scrutiny and warn that the amount and the duration of therapy should not exceed the amount and duration consistent with beneficial results.

Bronchiogenic Carcinoma and Pulmonary Asbestosis.—Holleb and Angrist report 2 cases of bronchiogenic carcinoma associated with pulmonary asbestosis. An attempt to demonstrate unusual amounts of silica in the lungs was unsuccessful: 240 mg. was present in the lungs of the first patient and 4.5 mg. in those of the second per hundred cubic centimeters of tissue. The silica content in the first patient was only slightly elevated, while that in the other one definitely fell within known nonpathologic limits. Therefore the diagnosis of pulmonary asbestosis must rest on (1) a history of prolonged exposure to the dust (twenty-five years for each patient), (2) the presence of a productive cough in 1 and of cough and severe exertional dyspnea without cardiac disease in the other and (3) evidence of asbestosis: diffuse interstitial pulmonary fibrosis, asbestosis bodies, macrophages and giant cells. Inhaled asbestos fiber undergoes dissolution and phagocytosis and may eventually disappear, but it leaves behind irreparable damage. As both patients were employed for a long time in an occupation in which the exposure to asbestos dust was relatively low, it is conceivable that extensive damage could result as a summation effect without an appreciable accumulation of asbestos in the lung.

American Journal of Psychiatry, New York

98:317-474 (Nov.) 1941. **Partial Index**

The Military Psychiatrist at Work. W. C. Porter, Washington, D. C.—p. 317.

*Clinical Differentiation of Senile and Arteriosclerotic Psychoses. D. Rothschild, Foxborough, Mass.—p. 324.

*Encephalopathia Alcoholica: Evaluation of Vitamin Therapy. N. Jolliffe and H. Wortis, New York.—p. 340.

Incidence and Significance of Alcoholism in History of Criminals. M. Geneva Gray and M. Moore, Boston.—p. 347.

Brain Metabolism: VIII. Effects of Electric Shock and Some Newer Drugs. S. M. Wortis, D. Shaskan, D. Impastato and R. Almansi, New York.—p. 354.

Insulin Convulsions: Method of Prevention. J. P. Frostig, San Francisco; C. R. Bennett, Camarillo, Calif.; J. Schreiber, Stockton, Calif., and G. F. Thomas, Camarillo, Calif.—p. 369.

Follow-Up Results in Insulin Shock Therapy After One to Three Years. T. D. Rivers and E. D. Bond, Philadelphia.—p. 382.

Vitamin B_1 Requirement During Insulin Shock Therapy. W. Goldfarb and K. M. Bowman, New York.—p. 393.

Treatment of Childhood Schizophrenia by Metrazol Shock Modified by B-Erythroidin. Frances Cottington, New York.—p. 397.

Effect of Convulsive Treatment on Memory. Irene Sherman, J. Mergener and D. Levitin, Chicago.—p. 401.

Electroencephalograms of Manic-Depressive Patients. Pauline A. Davis, Boston.—p. 430.

Mental Disorder in One of a Pair of Identical Twins. G. E. Hobbs, London, Ont., Canada.—p. 447.

Psychiatric Observations on Children with Abdominal Pain. J. P. Lambert, Katonah, N. Y.—p. 451.

Senile and Arteriosclerotic Psychoses.—Rothschild differentiates the two psychoses, seen in 60 cases, as follows: Senile psychosis tended to occur at a later age and was apt to last longer than arteriosclerotic psychosis. The course of the former was gradually progressive and of the latter sudden, and the illness was sometimes brief and stormy. Intellectual impairment was generally more pronounced in senile conditions. Depressive and hypochondriac symptoms were often observed in arteriosclerotic disease but seldom in senile disorders. Paranoid forms of senile psychosis resembled arteriosclerotic psychosis in that the intellectual functions were usually well preserved, but outspoken and chronic paranoid syndromes were not encountered in arteriosclerotic disease. Headache, dizziness and apoplectiform phenomena were observed in arteriosclerotic patients. Other characteristics were syncope, convulsions, explosive emotional outbursts and clinical indications of cardiac disturbances. Peripheral (radial) sclerosis and hypertension were observed with equal frequency in the two psychoses. Anatomically pure forms of each psychosis occurred less often than mixtures of the two processes, but clinically a mixed psychosis was not nearly as frequent. A diagnosis of senile or arteriosclerotic disease, especially of the latter, is made too often. A toxic or a symptomatic psychosis is a common source of error.

Alcoholic Encephalopathy.—Jolliffe and Wortis evaluate results of nutritional and vitamin studies in delirium tremens, the Korsakoff psychosis, Wernicke's syndrome and the various cerebral disorders due to deficiency of nicotinic acid. Dietary insufficiency as observed in chronic alcoholism is stressed. The effect of alcohol by itself has still to be evaluated. Vitamin therapy, to be effective, must be instituted before irreversible

structural changes occur. As in diseases of vitamin deficiency from other causes, those affecting the nervous system are usually the result of multiple rather than single deficiencies. Therefore a well balanced diet should supplement treatment with the specifically indicated vitamin or vitamins. Not all patients with the "encephalopathic syndrome" present the usual cutaneous and oral lesions associated with pellagra. Therefore it was assumed that the syndrome represents an acute complete nicotinic acid deficiency which sets in so rapidly that the structural changes characteristic of pellagra do not have time to develop. Patients with the syndrome who were treated by hydration or by hydration and with thiamine hydrochloride almost invariably died (95 per cent). Only half of those treated by hydration and with concentrates rich in the vitamin B complex died, but since such patients have been treated by hydration and with nicotinic acid the mortality has fallen to 15 per cent.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

46:765-918 (Dec.) 1941

Roentgen Kymography in Constrictive Pericarditis. L. G. Rigler, O. H. Wangensteen and H. L. Friedell, Minneapolis.—p. 765.
Attempt at Clinical Evaluation of Roentgen Kymography: Short Perspective Based on Six Years' Study. W. G. Scott, St. Louis.—p. 778.
Evaluation of Roentgen Kymogram in Study of Diseases of Heart and Great Vessels. M. M. Friedman, New York.—p. 784.
Cardiac Roentgenology: Value of Exact Cardiac Measurements. A. H. Clagett Jr., Wilmington, Del.—p. 794.
Roentgenographic Features of Perforated Interlobar Abscess (Interlobar Empyema). B. Copleman, Perth Amboy, N. J., and H. Neuhof, New York.—p. 798.
Pulmonary Manifestations of Azotemia. R. A. Rendich, A. H. Levy and A. M. Cove, Brooklyn.—p. 802.
Neuroblastoma and Its Roentgen Diagnosis: Report of Eight Cases. L. K. Chont, Oklahoma City.—p. 809.
Hodgkin's Disease Involving Stomach: Report of Two Cases. E. C. Koenig and G. J. Culver, Buffalo.—p. 827.
Intussusception: Report of Unusual Adult Case. A. X. Rossien, Kew Gardens, N. Y.—p. 832.
Structural Deformities of Spine Following Bilateral Laminectomy. T. Horwitz, Philadelphia.—p. 836.
Total Congenital Absence of Tibia. J. J. Nutt and E. E. Smith, New York.—p. 841.
*Treatment of Malignant Tumors of Testis. G. W. Chamberlin and J. H. Jamison, Philadelphia.—p. 850.
Effect of Vitamin B Complex Deficiency on Gastric Emptying and Small Intestinal Motility. G. W. Heublein, W. D. Thompson Jr. and J. P. Scully, Philadelphia.—p. 866.
*B_1 Avitaminosis: Roentgenologic Studies of Gastrointestinal Tract in Rats on Vitamin B_1 Deficiency Diets. J. Gershon-Cohen, H. Shay and S. S. Fels, Philadelphia.—p. 876.

Treatment of Malignant Tumors of Testis.—Chamberlin and Jamison state that malignant testicular tumors are not common; 45 were observed between December 1916 and December 1938 at the roentgen department of the University of Pennsylvania. The youngest patient was 18 and the oldest 74. For the purpose of irradiation these tumors are divided into radiosensitive and radioresistant types. Eleven of 12 patients who received irradiation followed by orchiectomy are living and well, as are 9 of 16 who had orchiectomy followed by irradiation and 3 of 17 who presented clinical evidence of abdominal metastasis when first seen. The patients who died did so within an average of twenty-four months after they were first seen. The proposed therapy for a patient with a primary testicular tumor is prompt diagnosis (by the aid of studies of the gonadotropic substance in the urine, excretory urograms and roentgen study of the tumor and chest) and preoperative irradiation over the lymphatics in the abdomen and then over the tumor. The response of the lesion to irradiation is sometimes a reliable diagnostic sign. If the tumor regresses orchiectomy should be done in a few weeks, and the chest and the supraclavicular region should be irradiated after the operation.

B_1 Avitaminosis.—Gershon-Cohen and his colleagues determined whether the intestinal motor activity is diminished in the rat by partial vitamin B_1 deficiency. After a sufficient interval of fasting measured quantities of a water-barium sulfate meal were introduced into the animal's stomach. The gastrointestinal motility of 8 normal animals varied. The stomach usually emptied in two hours (after a 3 cc. water-barium sulfate meal), but the time varied from one to three hours. The head of the column usually reached the cecum in four hours, but the time required varied from three to five hours. The colon was usually emptied in twenty-four hours. A decrease in the gastrointestinal motility was apparent within one month in the 8 rats fed a diet completely deficient in vitamin B_1 and after a longer period in those fed only partially deficient diets. The diets produced varying grades of atonicity and dilatation of the entire gastrointestinal tract. The changes observed are not accounted for by the mere loss of weight that occurred in the animals.

Am. J. Syphilis, Gonorrhea and Ven. Dis., St. Louis

26:1-132 (Jan.) 1942

Titration of Traces of Reagin: Technic of Flocculation Using Maximal Serum Proportions with Secondary Recovery of Antigen. H. Lund, Boston.—p. 1.
Infectiousness of Semen of Rabbits with Late Syphilis. J. E. Kemp, Baltimore.—p. 16.
*Management of Neurosyphilis. B. Dattner and E. W. Thomas, New York.—p. 21.
Report of Cooperative Plan for Rapid Appraisal of Chemotherapy of Gonorrhea in Male. O. F. Cox, Boston; Lida J. Usilton and R. W. Bowman, Washington, D. C.—p. 32.
*Culture Studies in Chronic Gonorrhea of Women. J. F. Mahoney, C. J. Van Slyke, R. R. Wolcott, J. D. Thayer, Staten Island, N. Y., and Anna Nimelman, New York.—p. 38.
Use of Sulfamethylthiazole and Sulfathiazole in Treatment of Gonococcic Urethritis in Male. P. R. Leberman, D. S. Pepper and C. M. Norfleet Jr., Philadelphia.—p. 48.
Comparison of Mediums and Laboratory Results in Gonococcus Cultures. C. J. Van Slyke, J. D. Thayer and J. F. Mahoney, Staten Island, N. Y.—p. 55.
Oral Administration of Arsphenamine and Neoarsphenamine in Treatment of Experimental Syphilis of Rabbits. J. A. Kolmer, H. Brown and Anna M. Rule, Philadelphia.—p. 63.
Congenital Syphilis: Statistical Study, with Special Regard to Sex Incidence. U. J. Wile and L. K. Mundt, Ann Arbor, Mich.—p. 70.
*Bismuth Stomatitis and Albuminuria: Report of Six Cases. E. E. Peters, Baltimore.—p. 84.
Distribution of Radioactive Arsenic in Normal and Tumor-Bearing (Brown-Pearce) Rabbit. Octavia du Pont, I. Ariel and S. L. Warren, Rochester, N. Y.—p. 96.

Management of Neurosyphilis.—Dattner and Thomas believe that in the treatment of syphilis it is less important to determine the sites affected than it is to determine the activity of the process and the kind of treatment that will check further progress. The clinical syndrome may be misleading; the most accurate information is to be obtained by a thorough examination of the spinal fluid. A positive Wassermann reaction of the spinal fluid in patients with untreated syphilis and with negative results of other tests does not prove activity. When a positive Wassermann reaction is associated with an increase in the number of cells or in the protein content of the spinal fluid, activity must be assumed. If there are no more than 3 or 4 cells per cubic millimeter of spinal fluid and the protein content is definitely decreased six months after treatment has been discontinued, the activity of the neurosyphilitic process has in all probability been checked permanently, although years may be required before the complement fixation and colloidal tests give negative results. A combination of chemotherapy and fever (malaria) therapy is the most effective treatment for all active neurosyphilis. Limiting the paroxysms of malarial fever to eight or nine reduces the danger of complications. Fever enhances the therapeutic effect of specific drugs and protects against their toxic action. The continued use of pentavalent or trivalent arsenicals after fever therapy is not necessary for most patients. Weekly injections following fever therapy should not be continued for more than six months unless there is an increase of cells and protein in the spinal fluid. If an increase does not occur, a rest period of six months is advised, after which another examination of the spinal fluid should establish whether the process has been checked permanently. The authors reduce the length of chemotherapy following fever to ten days by giving ten daily injections of 0.06 Gm. of mapharsen. Insufficient time has elapsed for a reliable evaluation, but so far study of the spinal fluid six months after all treatment was discontinued has proved most satisfactory.

Culture Studies in Chronic Gonorrhea.—Mahoney and his collaborators examined cervical secretions of 2,429 women of the prostitute class, of 73 untreated women with clinical evidence of gonorrhea and initially positive cultures and the pooled cervical and/or urethral secretions of 56 women to determine the efficacy of the cultural method for isolating the gonococcus. Most of the 2,429 women had varying degrees of cervicitis which might commonly be considered the result of gonococcic infection. A single culture of the cervical secretion revealed positive results in approximately 21 per cent. For each of the 73 patients at least ten and usually twenty culture plates were

used prior to the patient's release from custody. The cultures of 46 per cent remained positive throughout the study of three or four months; the cultures of the cervical secretion of 42 per cent remained positive for one or more observations and then abruptly or sometimes gradually they became negative and remained so during the remainder of the observation period; 12 per cent had characteristically positive cultures followed by numerous consecutive negative cultures and subsequently by one or more positive cultures occurring sporadically during the observation period. The pooled material of all the 56 patients showed the gonococcus, the cervical secretions of 53 and the urethral secretions of 23. A second cultural study was carried out on the secretions of 604 patients. A comparison of the results indicates that approximately one sixth of the patients whose original cultures were negative had positive cultures when the secretions were reexamined. Originally positive cultures were confirmed by reculture for only three fourths of the patients. The authors conclude that it may be unwise to withhold treatment from women solely on the basis of a negative culture when clinical and epidemiologic evidence of infection exists.

Bismuth Stomatitis and Albuminuria.—Peters states that the true incidence of the association of bismuth nephrosis or albuminuria with severe ulcerative stomatitis cannot be determined from the 6 cases recorded in the files of the Johns Hopkins Hospital. This is due partly to the failure in these cases to classify routinely the mild reactions to bismuth therapy and partly to the fact that when one complication was observed no attention may have been paid to the presence or the absence of the other one. In addition to the 6 patients who were hospitalized because of the severity of their complication, there were 7 with a similar but mild complication who were treated as outpatients. The work of Corson, Decker and Williams indicates that bismuth is mobilized by the administration of ammonium chloride. Peters suggests that it is probable that acidosis from any cause will lead to a mobilization of bismuth from the skeletal, muscular and visceral depots. That this may be possible is indicated by the test performed on 5 of the 6 patients who showed a lowered carbon dioxide combining power during the stomatitis and nephrosis. Bismuth should be administered cautiously to patients susceptible to acidosis, for example to patients with diabetes, previous renal damage, intercurrent infections, impaired food intake or retention and heart disease when ammonium chloride is given for its diuretic action. The acidosis which may result may cause bismuth to be mobilized to the extent of producing toxic phenomena.

Annals of Otol., Rhin. and Laryngology, St. Louis

50:979-1292 (Dec.) 1941. **Partial Index**

Leonardo da Vinci's Contribution to Laryngology, Rhinology and Phonetics. C. J. Imperatori, New York.—p. 979.
Choice of Treatment of Cancer in Otolaryngology. T. C. Galloway, Evanston, Ill.—p. 1018.
Functional Pattern of Autonomic Nervous System. D. Higbee, San Diego, Calif.—p. 1047.
Use of Preserved Human Cartilage in Reconstructive Facial Surgery. S. Iglauer, Cincinnati.—p. 1072.
Relation of Geriatrics to Otolaryngology. J. A. Babbitt, Philadelphia. —p. 1079.
Role of Nutrition in Industrial Hygiene. Agnes Fay Morgan, Berkeley, Calif.—p. 1114.
Infections of Masticator Space. C. Hall and F. Morris, Los Angeles. —p. 1123.
Otolaryngology from Immunologic Viewpoint. F. J. Novak Jr., Chicago. —p. 1134.
Further Modifications of Nasal Contact Test for Allergy. W. T. Vaughan and V. J. Derbes, Richmond, Va.—p. 1141.
Post-Traumatic Syndrome of Head Injury. H. A. Brown, San Francisco.—p. 1152.
Prophylaxis and Treatment of Common Cold, with Special Reference to Respiratory Vaccine. C. A. Veasey Jr., Spokane, Wash.—p. 1168.
*Chemotherapy and Serotherapy of Acute Otitis Media. R. N. Ganz, C. Lyons and C. F. Ferguson, Boston.—p. 1185.
Skin Reaction Controlled Low Dosage Method of Treatment with Staphylococcus Toxoid: Its Use in Certain Type of Acute Recurrent Rhinitis: Five Year Clinical Study of 394 Cases. K. E. Townsend, Detroit.—p. 1189.
Experimental and Clinical Study of Common Cold. I. G. Spiesman, Maywood, Ill.—p. 1204.

Chemotherapy and Serotherapy for Otitis Media.—According to Ganz and his associates, the early treatment of acute otitis media with myringotomy and sulfonamide derivatives supplemented with immune serum for patients who were not clinically convalescent within forty-eight hours prevented "surgical" mastoiditis in 40 patients with hemolytic streptococcus or pneumococcic infections. Experience for more than one year in more patients is necessary for a critical evaluation of the method, but the regimen appears most promising. Chemotherapy was continued, often in reduced doses, for three weeks for all patients.

Archives of Internal Medicine, Chicago

69:1-164 (Jan.) 1942

Type Specific Antibodies in Blood of Patients with Pneumococcic Pneumonia: Detection, Incidence, Prognostic Significance and Relation to Therapies. J. G. M. Bullowa, P. F. de Gara and S. C. Bukantz, New York.—p. 1.
Effect of Estrogen on Utilization of Vitamin B Complex. J. Ashworth and D. C. Sutton, Chicago.—p. 15.
Orthostatic Circulatory Insufficiency: Its Occurrence in Tabes Dorsalis and Addison's Disease. C. L. Spingarn and W. M. Hitzig, New York.—p. 23.
*Goiter with Associated Myasthenia Gravis: Report of Three Cases of Exophthalmic Goiter and One Case of Adenomatous Goiter with Hyperthyroidism. G. F. Kowallis, S. F. Haines and J. deJ. Pemberton, Rochester, Minn.—p. 41.
*Intravenous Use of Sodium Sulfadiazine in Treatment of Pneumococcic Pneumonia. A. H. Domm, H. F. Flippin, J. G. Reinhold and L. Schwartz, Philadelphia.—p. 51.
Infectious Neuronitis: Review of Literature and Presentation of Four Cases. M. J. Fox and R. D. O'Connor, Milwaukee.—p. 58.
*Serum Proteins in Cirrhosis of Liver: I. Relation to Prognosis and to Formation of Ascites. J. Post and A. J. Patek Jr., New York.—p. 67.
Id.: II. Nitrogen Balance Studies on Five Patients. J. Post and A. J. Patek Jr., New York.—p. 83.
Torula Meningitis. W. N. Warvi and R. W. Rawson, Boston.—p. 90.
Absorption of Intracutaneously Injected Solutions of Dextrose and Sodium Chloride: Comparison of Absorption Times for Diabetic and for Nondiabetic Subjects. M. Berg, Chicago.—p. 99.
*Prolonged Survival After Perforation of Infarcted Interventricular Septum in Coronary Arterial Disease. S. E. Moolten, New York.—p. 108.
Primary Portal Phlebosclerosis. N. E. Reich, Brooklyn.—p. 117.
Allergy: Review of Literature of 1941. F. M. Rackemann, Boston.—p. 128.

Goiter and Myasthenia Gravis.—According to Kowallis and his collaborators, subtotal thyroidectomy alleviated the symptoms of 1 of 4 patients with hyperthyroidism and myasthenia gravis of the bulbar type. When the two diseases coexist, either may easily be overlooked. The response to prostigmine of the patient with myasthenia gravis is an important diagnostic aid. Iodine may be administered as an aid in the diagnosis of exophthalmic goiter; however, in their patients its effect was not consistent. Its characteristic effect on exophthalmic goiter might not be obtained when untreated myasthenia gravis coexists. The basal metabolic rate, which is not elevated in the patient with uncomplicated myasthenia gravis, may be informative. Pathologically, both exophthalmic goiter and myasthenia gravis are associated with significant involvement of the thymus. The most favored theory of the origin of muscular weakness in myasthenia gravis suggests faulty transmission of nerve impulses due to a defect at the myoneural junction. When exophthalmic goiter and myasthenia gravis coexist, the goiter may precipitate the myasthenia in a patient with a latent tendency toward its development. Another, but less likely, possibility is that exophthalmic goiter may rarely produce muscular disturbances identical with those of myasthenia gravis. The prognosis for patients with the two diseases is grave, particularly if the myasthenia is of the bulbar type. Thyroidectomy for exophthalmic goiter complicated by myasthenia gravis offers certain difficulties. The patient must be able to dispose of tracheal mucus. In the instance reported by the authors, preoperative treatment with prostigmine resulted in sufficient improvement in muscular strength for them to feel no concern in this regard.

Sodium Sulfadiazine for Pneumococcic Pneumonia.—Domm and his associates gave 25 consecutive patients with pneumococcic pneumonia sodium sulfadiazine intravenously. Of the 25, 4 who represented extremely poor therapeutic risks died. There was no significant difference between the mortality with a dose of 2 Gm. given every twelve hours and that with 3 Gm. The results were comparable to those obtained by oral therapy with sulfadiazine. The administration of sodium sulfadiazine intravenously is to be used not as a routine but only when oral therapy is impracticable or impossible.

Serum Protein in Cirrhosis of Liver.—Post and Patek determined the albumin-globulin ratio of 61 and the nitrogen balance of 5 hospitalized patients with cirrhosis of the liver. Of the 61 patients, 54 had an abnormal albumin-globulin ratio on admission. The prognosis as to duration of life became increasingly grave as the level of serum albumin decreased. The level of the serum globulin and the value for total proteins in the serum had no such bearing. Clinical improvement was associated with a rise in the serum albumin level toward normal. In patients who failed to improve there was no sustained rise. The level of serum albumin was significantly lower in patients with ascites than in those without ascites. Diuresis was associated with a rise in serum albumin. The mean value for serum albumin at which diuresis occurred was 3.1 Gm. per hundred cubic centimeters. The nitrogen balance studies of the 5 patients revealed that although the patients remained in positive nitrogen balance during periods of high protein feeding there was no correlated rise in the level of the serum albumin. The data indicate that patients with cirrhosis of the liver absorb and retain food protein and that the mechanism for the synthesis of serum albumin is impaired.

Survival After Perforation of Infarcted Septum.—Moolten reports a case of survival for sixteen weeks after perforation of an infarcted interventricular septum in coronary arterial disease. During the twelve weeks after admission to the hospital (four weeks after the perforation) evidence of failure of the right side of the heart increased, despite treatment with digitalis and mercurial diuretics. From this case and a review of the histories of 3 similar ones the author concludes that the interventricular septum as a functional entity is of particular significance as a component of deep muscle tracts common to the two ventricles and as an agency for protecting the right ventricle by preserving the differential in pressure between the two ventricles.

Canadian Medical Association Journal, Montreal

46:1-110 (Jan.) 1942

Nutrition in Pregnancy. J. H. Ebbs, W. A. Scott, F. F. Tisdall, Winifred J. Moyle and Marjorie Bell, Toronto.—p. 1.
*Influence of Improved Prenatal Nutrition on the Infant. J. H. Ebbs, A. Brown, F. F. Tisdall, Winifred J. Moyle and Marjorie Bell, Toronto.—p. 6.
*Surgical Kidney as Etiologic Factor in Hypertension. W. F. Braasch, Rochester, Minn.—p. 9.
*Intracranial Use of Sulfadiazine: Experimental Study of Histology and Rate of Absorption. E. F. Hurteau, Montreal.—p. 15.
Closed Plaster Treatment of Recent Mastoid Wounds. J. Gerrie, Montreal.—p. 18.
Lower Uterine Segment: Anatomic Changes During Pregnancy and Labor. P. J. Kearns, Montreal.—p. 19.
Bacteriology of Recently Inflicted Wounds, with Special Reference to Hemolytic Streptococci and Staphylococci. R. Hare and Reba E. Willits, Toronto.—p. 23.
Method of Vaccine Therapy in Atrophic Arthritis. F. T. Cadham, Winnipeg, Man.—p. 31.
Character and Coincidence of Retinal Hemorrhages Occurring in Diabetes. F. T. Tooke and J. V. V. Nicholls, Montreal.—p. 35.
Present Status of Cyclopropane. R. M. Tovell and C. B. Hickcox, Hartford, Conn.—p. 41.
Cat Bite Wound Infection. A. E. Allin, Fort William, Ont.—p. 48.
*Acrodynia. U. J. Gareau, Regina, Sask.—p. 51.
Review of Medical Boards. R. W. I. Urquhart, Toronto.—p. 54.
Canada's Supply of Army Doctors. W. J. Deadman, Hamilton, Ont.—p. 60.
Resistance to Insulin. E. Lozinski and L. I. Frohlich, Montreal.—p. 62.

Antepartum Nutrition.—According to Ebbs and his associates, the infant mortality in Toronto has been reduced about 40 per cent in twelve years since indigent mothers have had their usual diet supplemented with milk, eggs, oranges, cheese, tomatoes, a wheat germ preparation and viosterol during their pregnancy. The number of premature deliveries, miscarriages and stillbirths has been reduced, and the general health of the newborn infants during the first six months of life has been singularly improved. The principles of nutrition are never more important than during pregnancy.

Surgical Kidney as Etiologic Factor in Hypertension.—From a review of the cases of hypertension observed at the Mayo Clinic Braasch concludes that a unilateral, non-nephritic, or "surgical," lesion of the kidney is not a frequent cause of hypertension and that the incidence of such lesions among patients with hypertension who are amenable to operation is less than 1 per cent. The removal of the unilateral renal lesion will often relieve hypertension. A urogram indicating deformity in the urinary tract does not necessarily mean that the renal lesion is an etiologic factor of the hypertension. Further urologic examination is necessary for an exact interpretation. There is no specific renal lesion in hypertension. The essential factor is apparently an intrarenal vascular imbalance which permits the secretion of pressor substances. The renal lesion in hypertension most often amenable to surgical treatment is chronically unilateral, diffuse, atrophic or postoperative pyelonephritis. The deciding factor in the presence of secondary infection is not the degree of infection but the consequent lesions in the renal parenchyma which cause intrarenal secretion of pressor substances. Hypertension was observed less frequently with renal tuberculosis than as an accompaniment of other forms of surgical kidney. Bilateral renal involvement was not an etiologic factor in hypertension. A follow-up study of 198 patients who were operated on revealed that the blood pressure of 65 became and remained normal for a year or more.

Intracranial Use of Sulfadiazine.—Hurteau observed in 9 cats that the local application to a cerebral wound of several drugs of the sulfonamide group resulted in different rates of absorption. The rate was determined by extraction and chemical analysis. Sulfanilamide was absorbed most rapidly, sulfathiazole second and sulfadiazine third, and sulfapyridine was absorbed the least rapidly. Sulfadiazine when in contact with meninges or cerebral parenchyma caused no neuronal destruction and no glial reaction and only a negligible foreign body reaction in the meninges. Sulfadiazine exercised no untoward effect on the final result of wound healing.

Acrodynia.—Gareau reports 75 cases of acrodynia encountered in nine years: 17 from cities, 17 from smaller centers and 41 from farms; 30 were in males and 45 in females. The incidence was highest from December to June. The average age at onset was a little more than 11 months. There was a family history of acrodynia in four families, one family having had 3 children with the disease and three families having had 2 each. Two families lost a child each from complications. Most parents dated the onset of illness to some antecedent illness. The most frequent complaints were fretfulness, irritability and unhappiness, loss of ability to sit, stand and walk, sore eyes, loss of weight, sleeplessness and rash, while the least frequent complaints were profuse sweating, loss of teeth and fever. Four patients died (1 from bronchopneumonia and endocarditis and 3 from bronchopneumonia); 71 recovered, and of these 3 were not seen after the first examination. Of the remaining 68, 57 had their tonsils and adenoids removed. For the 11 not operated on the average duration of illness was about seven months. Of the 57 operated on 30 recovered rapidly, the average duration of illness being less than three and a half months. The 4 patients who died did so before the advent of modern chemotherapy. Etiologic factors that have been suggested as causes of acrodynia are a lesion in the diencephalon or mesencephalon similar to encephalitis, vitamin deficiency, smut infected cereals, hypervitaminosis D from sunlight, arsenical poisoning, allergy and infection. The average duration of acrodynia is about six months. It is suggested that acrodynia is due to a toxemia caused by infected tonsils and adenoids.

Canadian Public Health Journal, Toronto

32:587-630 (Dec.) 1941

Canada's War Effort for the Health of Her People. J. J. McCann, Renfrew, Ont.—p. 587.
Study of 345 Family Contacts with Tuberculous Lesions. H. J. Anderson, Fort Qu'Appelle, Sask.—p. 594.
Value of Annual Report of Medical Officer of Health. J. E. Davey, Hamilton, Ont.—p. 601.
*Pediculosis—New Treatment. L. P. MacHaffie, Ottawa, Ont.—p. 606.
High School Medical Inspection in Burlington, Ont. A. H. Speers, Burlington, Ont.—p. 608.
Fallacy of Calculating Rates of Births and Deaths According to Place of Occurrence. E. Gagnon, Montreal.—p. 611.

Pediculosis.—For the cure of pediculosis MacHaffie recommends 15 per cent of lethane (n butyl-carbitol-thiocyanate) in deodorized purified kerosene. One treatment applied to the head without a towel covering kills nits and lice immediately. The head is not to be shampooed for a few days. The cost per head is not more than 2 or 3 cents.

Connecticut State Medical Journal, Hartford

6:1-78 (Jan.) 1942

Influence of Food, Drug and Cosmetic Act on Marketing of Drugs. T. G. Klumpp, New York.—p. 3.
Treatment of Fresh Wounds. R. H. Kennedy, New York.—p. 9.
*Use of Normal Human Plasma in Armed Forces. L. R. Newhouser and E. L. Lozner, Washington, D. C.—p. 14.
Supplementary Revenue, Subsidies, Gifts, Donations, Endowments and Other Sources of Financial Support. O. H. Bartine, Bridgeport. —p. 17.
Tonsillectomy in Selected Peritonsillar Abscess: Case Reports and Commentary. F. Turchik, Bridgeport; N. Canfield, F. N. Sperry, New Haven; P. W. Snelling, E. J. Whalen, Hartford; S. H. Baron, New London, and W. H. Turnley, Stamford.—p. 25.
Sesquicentennial Celebration. H. Thoms, New Haven.—p. 26.
Connecticut State Medical Society and Medical Institution of Yale College. H. S. Burr.—p. 28.

Use of Normal Human Plasma.—Newhouser and Lozner state that an enrolment of two hundred thousand donors by the American Red Cross has been raised since the United States declared war on the Axis. The medical profession can aid in the collection of a vast amount of plasma by informing patients who can give blood to do so and by allaying their apprehension of venesection. Unless vasoconstriction, hemoconcentration, venous stasis, decreased blood flow, anoxia of tissue and increased capillary permeability following injuries are promptly interrupted the changes in the tissues will be irreversible and the termination fatal. The prompt administration of an adequate amount of normal human plasma not only will halt but will reverse this sequence of events. Death from hemorrhage is due not to the loss of erythrocytes but to the decrease in the circulating blood volume. Plasma is superior to whole blood, since it promptly corrects the increased viscosity of the blood and restores the circulating blood volume. Plasma, preserved in the liquid, frozen or dried state, has the advantage over blood that it can be administered safely without typing of the donor or of the recipient and without preliminary cross matching. Liquid plasma is safe and is most economical if prepared by a closed aseptic and pyrogen free method and if used before the lapse of nine months of storage at 10 to 20 C. After it has been stored eight to nine months a progressive loss of prothrombin, complement and possibly other labile constituents occurs. Liquid plasma is satisfactory for use in hospitals, but it is not well adapted for use aboard ship, in the field of combat or in bases beyond continental limits, where longer periods of storage may be necessary. For use in the foregoing situations frozen plasma (kept at —15 to —20 C.) is ideal, as all the labile constituents are preserved indefinitely, but it must be thawed to or near body temperature, and this may not always be convenient. The restoration of properly dried plasma to the liquid state takes less than three minutes. The time consuming, complicated and expensive method necessary to prepare dried plasma is offset by the facts that it is stable indefinitely, that it survives extreme changes in temperature and that when properly packaged it is ideal for use in the field and aboard ship. For this reason the armed services have decided to use the dried form. The standard army and navy package contains a bottle of dried plasma (made from 300 cc. of citrated plasma), a bottle (300 cc.) of sterile pyrogen free distilled water and the apparatus necessary for restoration and administration. After the torpedoing of the U. S. S. *Kearny*, dried plasma was flown to and dropped by parachute to the medical officer on board ship.

Florida Medical Association Journal, Jacksonville

28:253-308 (Dec.) 1941

Conditions Simulating Appendicitis. F. G. Slaughter, Jacksonville.—p. 265.
Rickettsial Disease in the South. J. O. W. Rash, Miami.—p. 270.
The Public Health Control of Gonorrhea. L. C. Gonzalez, Jacksonville. —p. 286.
Three Cases of Cancer in Children Under Three Years of Age. H. E. Palmer, Tallahassee.—p. 289.

28:309-360 (Jan.) 1942

Use of Vitamins in Surgery. J. R. Chappell, T. Butt and S. L. Zieve, Orlando.—p. 323.
Modern Methods of Immunization. T. M. Palmer, Jacksonville.—p. 330.
A Year's "Eye" Service at Florida State Hospital in Retrospect. F. V. Gammage, Chattahoochee.—p. 333.
Plea for Conservative Treatment of Inevitable and Incomplete Abortion. W. C. Roberts, Panama City.—p. 338.

Georgia Medical Association Journal, Atlanta

30:493-534 (Dec.) 1941

Xeroderma Pigmentosum: Report of Case. E. Bosworth, Rome.—p. 493.

31:1-40 (Jan.) 1942

Women in Medicine. Loree Florence, Athens.—p. 1.
Sparta Child Health Demonstration: Review of Organization, Plans, Activities and Accomplishments. T. F. Abercrombie, Atlanta.—p. 15.
Refractory Psoriasis: Report of Attempt to Clear Resistant Lesions by Intramuscular Injection of Vitamin D. J. Krafka Jr., Augusta. —p. 21.

Illinois Medical Journal, Chicago

81:1-80 (Jan.) 1942

Scarlet Fever. A. L. Hoyne, Chicago.—p. 12.
Ileocecal Granulomas. F. L. McMillan, Chicago.—p. 15.
*Tumors Occurring in Region of Pulmonary Apex: Further Observations with Report of Twelve Additional Cases. J. J. Stein, Hines.—p. 21.
*Five Day Treatment of Syphilis. H. Rattner, Chicago.—p. 29.
*Paravertebral Alcohol Injection for Relief of Cardiac Pain. S. Perlow, Chicago.—p. 35.
Rheumatism: Practical Methods of Study and New Phases of Investigation. W. L. Wood, R. Merchant, Lucille Watt and Elizabeth Belting, Chicago.—p. 41.
Physiologic Problems in Suction Drainage of Gastrointestinal Tract. J. L. Lindquist, Chicago.—p. 49.
Favorable Prognosis of Coronary Disease. D. Luten, St. Louis.—p. 52.
Vitamin K in Hypoprothrombinemia. J. E. Karabin, Evanston.—p. 56.
Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian Disease). W. A. Rosenberg and T. M. Cohen, Chicago.—p. 59.
Acute Perforation of Gastric and Duodenal Ulcer: Study of 200 Consecutive Operated Cases. J. B. O'Donoghue and M. B. Jacobs, Chicago.—p. 62.
Incidence of Syphilis in Alcoholic Patients: Statistical Study of 760 Consecutive Cases. A. J. McGee, Dwight.—p. 69.
Diagnosis of Poliomyelitis. B. M. Levin, W. H. Reals, I. P. Bronstein and M. Magree, Chicago.—p. 71.

Tumors in Region of Pulmonary Apex.—Stein reviews 15 cases of so-called tumor of the superior pulmonary sulcus which he reported in 1937 and 1938 and presents 12 new cases. Only 1 of the 15 patients was a Negro, and all were men. The right lung of 10 and the left of 5 was involved. The duration of life from the onset of symptoms was thirteen and four-tenths months. The first symptom was pain in the shoulder and arm on the affected side. Horner's syndrome was present in 13 and costal or vertebral changes in 11. Nine patients were irradiated with no appreciable effect; in 2 an attempt was made to remove the tumor, but because the mediastinum and the brachial plexus were involved this was not possible. Eleven of the twelve new tumors occurred in white men and one in a Negro. The average age on admission was 50.7 years. The right lung of 7 patients and the left lung of 5 was involved. The first symptom in 11 was pain in the shoulder on the affected side; Horner's syndrome was present in 8 and costal or vertebral changes in the apical region in 7. Ten patients were irradiated with no appreciable relief, in 1 irradiation and the injection of alcohol into the involved sympathetic nerves gave some relief and 1 obtained relief from symptomatic therapy only. All the patients have died; the average length of life from the onset of symptoms was twelve and three-tenths months. Although Pancoast in 1932 expressed the belief that he had described a new pathologic and clinical entity, recent evidence shows that any tumor in the pulmonary apex may produce the syndrome that he described. The evidence on which he based his conclusions is inadequate, especially since gross or postmortem evidence was not available, a branchial origin has not been demonstrated and no anatomic structure has been designated as the superior pulmonary sulcus. Microscopic and postmortem evidence is presented which shows that the majority of the malignant tumors in the thoracic inlet or pulmonary apex are carcinomas of the terminal bronchioles of the lung.

Five Day Treatment of Syphilis.—Rattner reports 170 cases of early syphilis in which the so-called five day therapy was employed. The daily dose amounted to 0.24 Gm. of mapharsen dissolved in 2,000 cc. of a 5 per cent solution of dextrose in triple distilled water. There were 103 men and 67 women; 52 had primary syphilis and 118 presented secondary manifestations. Final clinical evaluation cannot yet be made, because experience is much too recent. Spirochetes disappeared from the lesions usually in one or two days, and all open lesions healed during the seven days of hospitalization.

The spinal fluid of 162 patients was examined and was found normal in each instance. Eighty patients have been observed for five or more months after the completion of treatment. All relapses occurred in the fourth month. Of the first 80 patients 14 had to be dropped from the study, in 28 the blood serologic reactions reverted from positive to negative (usually in the tenth week), in 2 the Kahn reaction is still positive six months after treatment but the Kahn quantitative units are steadily decreasing, in 6 (treated before the serologic reaction of the blood became positive) the reaction is still negative after eight months and in 18 a progressive improvement was demonstrated by Kahn quantitative tests; 3 of the remaining patients have relapsed, 1 has probably relapsed or become reinfected, 2 have had reinfection and in 6 the results were "unsatisfactory when the patient was last seen" (the blood quantitative titers were vacillating rather than decreasing).

Paravertebral Injection of Alcohol for Cardiac Pain.—Perlow states that 16 of 22 patients with cardiac pain obtained complete or partial relief from pain after a paravertebral injection of alcohol. The method is simple and relatively safe and can be repeated if necessary. The objection that the injection removes the danger signal (pain) of coronary insufficiency is theoretical. The patient soon learns to heed other signals and does not harm himself. The relief of pain not only is symptomatically desirable but actually reduces the work of the heart, as the patient can rest and relax.

Journal of Clin. Endocrinology, Springfield, Ill.

2:1-64 (Jan.) 1942

Creatinine Excretion in Women: Data Collected in Course of Urinalysis for Female Sex Hormones. O. W. Smith, Brookline, Mass.—p. 1.
Creatine Retention Capacity of Boys in Relation to Androgen Function. D. A. Duckworth, New York.—p. 13.
Effects of Testosterone Propionate and Stilbestrol on Mammary Gland Postpartum. E. M. Jeppson, Salt Lake City; H. Y. Kasabach and A. E. Kanter, Chicago.—p. 16.
Stilbestrol Monomethyl Ether: Report on Its Clinical Use. C. F. Geschickter and Elizabeth W. Byrnes, Baltimore.—p. 19.
*Clinical Experiences with Sublingual Administration of Alpha Estradiol. G. J. Hall, Sacramento, Calif.—p. 26.
*Sexual Infantilism of Hypothyroid Origin. H. Lisser, San Francisco. —p. 29.
*Carotenemia in Myxedema: Explanation of Typical Slightly Icteric Tint. R. F. Escamilla, San Francisco.—p. 33.
Diagnosis of Addison's Disease. J. M. Rogoff, Pittsburgh.—p. 36.
Treatment of Addison's Disease with Interrenalin (Adrenal Cortex Extract). J. M. Rogoff, Pittsburgh.—p. 43.
Effect of Adrenal Cortical Extract, Desoxycorticosterone and Added Potassium on Electrolyte Balance in Normals and in Addison's Disease. J. A. Greene, Ann David and G. W. Johnston, Iowa City.—p. 49.
Preoperative Administration of Desoxycorticosterone Acetate in Prevention of Surgical Shock. F. R. Keating Jr., E. H. Rynearson and Marschelle H. Power, Rochester, Minn.—p. 53.

Sublingual Administration of Alpha Estradiol.—Hall compared the absorption ratio of alpha estradiol in a solution of propylene glycol-alcohol administered sublingually to that of alpha estradiol benzoate given intramuscularly to 98 women with menopausal symptoms. In 41 patients the variation in vaginal cornification after sublingual therapy was determined over fourteen days. At the end of this time, castrates who had received no previous therapy showed improved vaginal cornification, 15 women in the menopause showed a slight reduction of cornification, 8 had smears showing an improved estrogenic level, 5 who had had a hysterectomy had a slight reduction and 3 were definitely improved. Twenty-four of 41 patients did not maintain the same estrogenic level, 3 maintained the original high level and 14 showed much improvement. The patients who did not maintain the required level of estrogen were given an intramuscular injection of 10,000 rat units of estradiol benzoate followed by a dose of 0.1 cc. of the estradiol solution, given sublingually, five times a day (instead of the usual four) with completely adequate results. Therefore, individualization of the dose is required for effective clinical results with sublingual administration. The data justify the belief that the giving of alpha estradiol in a propylene glycol-alcohol solution sublingually produces the same effects on vaginal cornification as the giving of estradiol benzoate parenterally. Propylene glycol-alcohol solution appeared as effective, milligram for milligram, as did alpha estradiol benzoate given hypodermically.

Sexual Infantilism of Hypothyroid Origin.—Lisser reports a case in which the manifestations suggested adolescent hypothyroidism without typical myxedema. An unmarried woman of 27, who appeared twelve to fifteen years younger and whose secondary sexual characteristics were undeveloped, had had irregular, scanty menstrual periods since the age of 16. She was somewhat below normal height, her bone age was estimated at 14 years, her features were slightly puffed and she had a pulse rate of 58 to 66, a basal metabolic rate of —27, severe anemia, preference for warm weather and easy fatigability. The patient was treated for one year with thyroid. This elevated the basal metabolic rate to normal, diminished the anemia and caused the breasts to develop, the menstrual periods to become regular and the personality to become vivacious. She has married and has experienced intense libido and gratification. The pubic hair remained sparse, and no axillary hair appeared. Diethylstilbestrol (1 mg. daily, given orally) was used later, and this seemed to stimulate the growth of the pubic hair.

Carotenemia in Myxedema.—Escamilla cites 7 consecutive cases of untreated myxedema in which carotenemia coexisted. He suggests that this may be part of the typical clinical picture and may explain the yellowish color of the skin seen so frequently. The carotenemia cleared gradually under treatment with thyroid substance. Carotenemia was observed also in a patient with Simmonds' disease. It is suggested that carotenemia frequently accompanies a low basal metabolic rate. The probable explanation is that the conversion of carotene to vitamin A in the liver is hindered by the depressing effect of the lowered metabolism.

Journal of Clinical Investigation, New York

21:1-120 (Jan.) 1942

Cardiocirculatory Effects in Man of Neosynephrin (1-α-Hydroxy-β-Methylamino-3-Hydroxy-Ethylbenzene Hydrochloride). A. Keys and A. Violante, Minneapolis.—p. 1.
Cardiocirculatory Effects in Man of Synephrin Tartrate (dl-α-Hydroxy-β-Methylamino-4-Hydroxy-Ethylbenzene Hydrochloride). A. Keys and A. Violante, Minneapolis.—p. 13.
Changes in Blood Pressure and in Renal Blood Flow and Glomerular Filtration Rate of Hypertensive Patients Following Unilateral Nephrectomy. M. Friedman, A. Selzer, H. Kreutzmann and J. J. Sampson, with technical assistance of P. Blakeslee, San Francisco.—p. 19.
Radioactive Iodine as Indicator in Thyroid Physiology: IV. Metabolism of Iodine in Graves's Disease. S. Hertz, A. Roberts and W. T. Salter, Boston.—p. 25.
Id.: V. Use of Radioactive Iodine in Differential Diagnosis of Two Types of Graves's Disease. S. Hertz and A. Roberts, Boston.—p. 31.
Rôle of Adrenal Cortex in Acute Anoxia. R. A. Lewis, G. W. Thorn, G. F. Koepf and S. S. Dorrance, Baltimore.—p. 33.
*Effects of Interrupting and Restoring Circulation to Lower Extremities. D. Dauber, M. Landowne, L. N. Katz and H. Weinberg, Chicago. —p. 47.
Filtration Rate, Effective Renal Blood Flow, Tubular Excretory Mass and Phenol Red Clearance in Normal Pregnancy. Catherine A. Welsh, I. Wellen and H. C. Taylor Jr., with technical assistance of Anna Rosenthal, New York.—p. 57.
Filtration Rate, Effective Renal Blood Flow, Tubular Excretory Mass and Phenol Red Clearance in Specific Toxemia of Pregnancy. I. Wellen, Catherine A. Welsh and H. C. Taylor Jr., with technical assistance of Anna Rosenthal, New York.—p. 63.
Prevention of Sensory Neuron Degeneration in Pig, with Special Reference to Role of Various Liver Fractions. M. M. Wintrobe, C. Mushatt, J. L. Miller Jr., L. C. Kolb, H. J. Stein and H. Lisco, Baltimore. —p. 71.
Pathologic Variations in Blood and Spinal Fluid Pyruvic Acid. E. Bueding, H. Wortis and M. Stern, with technical assistance of Dorothy Esturonne, New York.—p. 85.
*Significance of Porphyrinuria in Lead Poisoning. R. Kark and A. P. Meiklejohn, Boston.—p. 91.
Acid-Base Balance of Premature Infants. W. S. Branning, Durham, N. C.—p. 101.
Renal Function in Patients with Addison's Disease and in Patients with Adrenal Insufficiency Secondary to Pituitary Panhypofunction. J. H. Talbott, L. J. Pecora, R. S. Melville and W. V. Consolazio, Boston.—p. 107.

Circulation to Lower Extremities.—Dauber and his associates studied the changes in cardiac acceleration and arterial and venous pressure that occurred during the release of a tourniquet applied to the extremities and during occlusion in 27 normal young adults and in 4 subjects with moderately advanced thromboangiitis obliterans. The observations were made while the subjects were recumbent, after a rest period of fifteen to thirty minutes in a warm quiet and darkened room. Cardiac acceleration followed release of occluding cuffs in the

normal subjects but was absent or reduced in the patients with thromboangiitis obliterans. A fall of the blood pressure in the brachial artery preceded the cardiac acceleration. The fall in blood pressure was caused by the opening of a temporary low resistance pathway for blood through vessels dilated as a result of the previous occlusion. The primary mechanism inducing the cardiac acceleration is a reflex response to the drop in pressure in the central arteries (Marey's law). The cardiac acceleration is not caused by a metabolite accumulating in the constricted extremities. The assumption that the reflex arises from the occluded vessel or from the tissue of the extremity is not satisfactory.

Porphyrinuria in Lead Poisoning.—Kark and Meiklejohn attempted to trace the path of the destruction of hemoglobin in 2 cases of lead poisoning by observing the effect of intravenously injected hemoglobin on the production of bilirubin and on the excretion of coproporphyrin and urobilinogen in the urine and feces. The introduction of free hemoglobin was followed by a rapid rise in plasma bilirubin. This resembled the bilirubinemia observed by Gilligan, Altschule and Katevsby in normal subjects under the same conditions. It was accompanied by a transient increase in the excretion of urinary urobilinogen. The injection caused no detectable increase in the urinary or fecal excretion of coproporphyrin. An interruption in the path by which hemoglobin is destroyed in the body was not demonstrated. Therefore the porphyrinuria occurring in lead poisoning cannot be explained on this basis. The results lend support to the view that the anemia in lead poisoning is dyshemopoietic rather than hemolytic.

Journal Industrial Hygiene & Toxicology, Baltimore

23:459-496 (Dec.) 1941

Significance of Urinary Mercury: I. Occupational Mercury Exposure: II. Mercury Absorption from Mercury Bearing Dental Fillings and Antiseptics. E. D. Storlazzi and H. B. Elkins, Boston.—p. 459.
Phenylmercuric Oleate: Skin Irritant Properties. C. P. McCord, S. F. Meek and T. A. Neal, Detroit.—p. 466.
Toxicology of Selenium: VI. Effects of Subacute Exposure to Hydrogen Selenide. H. C. Dudley and J. W. Miller, Bethesda, Md.—p. 470.
Some Pharmacologic Properties of "Tergitol" Penetrants. H. F. Smyth Jr., Jane Seaton and Louise Fischer, Pittsburgh.—p. 478.
Solubility of Carbon Disulfide Vapor in Body Fluids and Tissues. R. W. McKee, Boston.—p. 484.

24:1-20 (Jan.) 1942

Evaluation of Lead Hazard in Decorating Department of Glass Plant: Relation of Urinary and Atmospheric Lead Determinations. C. A. Smucker and J. B. Kistler, Columbus, Ohio.—p. 1.
Metabolism of Mononitroparaffins: I. Recovery of Nitroethane from Animal Organism. W. Machle, E. W. Scott and J. Treon, Cincinnati.—p. 5.
Determination of Formaldehyde in Air. E. C. Barnes and H. W. Speicher, East Pittsburgh, Pa.—p. 10.

Journal of Investigative Dermatology, Baltimore

4:431-524 (Dec.) 1941

Electrolyte Content and Permeability of Erythrocyte in Pemphigus. N. B. Kurnick, W. F. Lever and J. H. Talbott, Boston.—p. 431.
Donnan Equilibrium and Blister Formation. T. Cornbleet, Chicago.—p. 451.
Dermatitis from New Synthetic Resin Fabric Finishes. L. Schwartz.—p. 459.
Practical Application of Some Immunologic Principles to Diagnosis and Treatment of Certain Fungous Infections. D. S. Martin, Durham, N. C.—p. 471.
Pigment Studies in Skin Grafts on Experimental Animals. M. L. Lewin and S. M. Peck, New York.—p. 483.
Studies in Eczematous Sensitizations: I. Comparison Between Sensitizing Capacities of Two Allergens and Between Two Different Strengths of Same Allergen and Effect of Repeating Sensitizing Dose. A. Rostenberg Jr. and Naomi M. Kanof, Washington, D. C.—p. 505.

Journal of Nervous and Mental Disease, New York

95:1-132 (Jan.) 1942

Abstract Art as Expression of Human Problems. P. Schilder and Esther Leepa Levine, New York.—p. 1.
Exhibitionism. N. K. Rickles, Seattle.—p. 11.
Pharmacologic Aspects of Shock Therapy. H. A. Hoffman, Washington, D. C.—p. 18.
Obsessive-Compulsive Neurosis in Children. L. Berman, Boston.—p. 26.
Intravenous Injection of Solution of Zinc Insulin Crystals: Its Effect in Treatment of Mental Diseases. P. Polatin, H. Spotnitz and A. J. Raffaele, New York.—p. 40.
Problems of "Physiologic" Sense Perception. M. Marquardt, Augusta, Maine.—p. 46.

Journal of Neurophysiology, Springfield, Ill.

5:1-88 (Jan.) 1942

Electric Potential Changes at Isolated Nerve Muscle Junction. S. W. Kuffler, Sydney, Australia.—p. 18.
Responses of Iris to Prolonged Stimulation of Its Parasympathetic Nerve Supply. J. V. Luco and H. Salvestrini, Santiago, Chile.—p. 27.
Isolation of Retinal and Optic Ganglion Response in Eye of Dytiscus. C. G. Bernhard, Stockholm, Sweden.—p. 32.
Acoustic Area of Monkey (Macaca Mulatta). H. W. Ades, Atlanta, Ga., and R. Felder.—p. 49.
Breakdown of Accommodation—Nerve as Model Sense Organ. C. G. Bernhard, R. Granit and C. R. Skoglund, Stockholm, Sweden.—p. 55.
Effect of Section of Medial Lemniscus on Proprioceptive Functions in Chimpanzees and Monkeys. O. Sjöqvist and E. A. Weinstein, New Haven, Conn.—p. 69.
Excitation and Inhibition of Phrenic Motor Neurons. R. F. Pitts, New York.—p. 75.

Journal of Nutrition, Philadelphia

23:1-100 (Jan.) 1942. **Partial Index**

Utilization of Calcium of Carrots by Adults. Herta Breiter, Rosalind Mills, Esther Rutherford, Williamina Armstrong and Julia Outhouse, Urbana, Ill.—p. 1.
Occurrence of Free and Bound Biotin. J. O. Lampen, G. P. Bahler and W. H. Peterson, Madison, Wis.—p. 11.
Studies in Nicotinic Acid Metabolism: Parts I and II. H. P. Sarett, J. W. Huff and W. A. Perlzweig, with technical assistance of Molly Stenhouse and Rachel Forth, Durham, N. C.—p. 23.
Pantothenic Acid in Nutrition of Rat. L. M. Henderson, J. M. McIntire, H. A. Waisman and C. A. Elvehjem, Madison, Wis.—p. 47.
Criteria of Response in Bioassay of Vitamin E. K. E. Mason, Nashville, Tenn.—p. 59.
Distribution of Vitamin E in Tissues of Rat. K. E. Mason, Nashville, Tenn.—p. 71.

Journal of Pediatrics, St. Louis

20:1-144 (Jan.) 1942

Whooping Cough: Parts I to IV. N. Silverthorne, C. Cameron and A. Brown, Toronto, Canada.—p. 1.
Stimulation Dose in Whooping Cough. J. H. Lapin, Bronx, N. Y.—p. 18.
Infectious Mononucleosis: Its Treatment with Scarlet Fever Convalescent Serum. H. K. Berkley, Los Angeles.—p. 26.
*Comparison of Routine Urinalysis, Addis Count and Blood Sedimentation Rate as Criteria of Activity in Acute Glomerulonephritis. M. I. Rubin, M. Rapoport and A. D. Waltz, Philadelphia.—p. 32.
*New Concepts of Gonococcic Vaginitis. A. Cohn, A. Steer and Eleanor L. Adler, New York.—p. 41.
Tuberculin Patch Test: Study of Effect of Variations of Normal Procedures. J. Schwartzman, D. Dragutsky and G. Rook, Brooklyn.—p. 50.
Benzedrine Sulfate (Amphetamine) in Treatment of Obese Children and Adolescents. Hilde Bruch and Irene Waters, New York.—p. 54.
Thiamine Content of Various Milks. N. Kendall, Philadelphia.—p. 65.
*Truncus Arteriosus Communis Persistens. M. Lev and O. Saphir, Chicago.—p. 74.
Mercury Poisoning from Topical Application of 15 per Cent Ammoniated Mercury: Report of Case. C. L. Wilbar Jr., Honolulu, Hawaii.—p. 89.
Feeding Behavior of Infant During First Twelve Weeks of Life on Self-Demand Schedule: Narrative by Mother with Discussion by Pediatrician. Frances P. Simsarian and P. A. McLendon, Washington, D. C.—p. 93.
*Incidence of Tuberculosis Among 2,562 High School Students in Suburban City. W. B. Nevius, East Orange, N. J.—p. 104.

Urinalysis, Addis Count, Blood Sedimentation Rate.—Rubin and his associates followed the course of an attack of acute glomerulonephritis in 40 patients hospitalized within five days of its onset by means of determination of the blood sedimentation rate and the Addis count and routine urinalysis. The data show that while routine urinalysis usually gave normal results on the thirty-seventh day the Addis count required one hundred and twenty days to become normal. There was a close correlation between the number of days required for the twelve hour erythrocyte excretion (Addis count) to drop to the 10 million level (seventy-six days) and the time necessary for the rapid sedimentation rate to become normal (eighty-six days). The data demonstrate the inadequacy of routine urinalysis as a guide to the cessation of active disease. The simplicity of the determination of the blood sedimentation rate makes the test a valuable index of the course of acute glomerulonephritis.

New Concepts of Gonococcic Vaginitis.—During the last three years Cohn and his colleagues examined 1,715 girls who had symptoms of gonococcic vaginitis or were contacts of persons with the disease. The cultures and smears of only 381 were positive. The culture method was the best for the

diagnosis and the pronouncement of cure of gonococcic vaginitis. Sulfathiazole therapy was the treatment of choice. Patients with vaginitis who require hospitalization may be cared for in general wards when the usual isolation technic applied for other slightly communicable diseases is employed. Treated patients may return to schools and institutions when clinical signs have cleared up and the cultures are negative. Cure may be pronounced satisfactory when culture gives a negative result every month for six months. Vaginitis will not spread from one girl to another when the vaginal discharge of an infected child is prevented from reaching the vulva of a noninfected one. Attention should be directed toward contaminated linen, diapers, rectal thermometers, enema tips and the fingers of the parent or attendant. The last mentioned item is probably most frequently the fomes in the transmission of the disease. Toilet seats are not an important factor.

Truncus Arteriosus Communis Persistens.—Lev and Saphir observed a girl baby aged 18 days whose heart was the seat of a transposition with truncus arteriosus communis persistens. The anatomic features of the case were as follows: 1. Only one large vessel, arising from the right ventricle, emanated from the heart. This trunk gave off the coronary arteries, the systemic vessels and two pulmonary arteries. 2. The mouth of this vessel was guarded by three semilunar cusps. 3. The right and left coronary ostiums lay, respectively, in the sinus of Valsalva of the left anterior cusp adjacent to the right anterior cusp and above the commissure between the posterior and right anterior cusps. 4. There was an archlike ridge over the combined mouths of the pulmonary arteries. 5. No vessel emerged from the left ventricle. 6. There was a defect of the ventricular septum. 7. The right auriculoventricular valve had only two leaflets. 8. The foramen ovale was patent. 9. The anatomy of the muscle bundles of the right ventricle was abnormal. The authors present a phylogenic and embryologic explanation of the anomaly.

Tuberculosis Among High School Students.—Nevius states that the patch testing of 2,562 high school students disclosed 396, or 15 per cent, who reacted positively. Roentgenograms of the 396 students showed that 66 had the primary complex and 6 the reinfection type of the disease. The cost of the testing and of making the necessary roentgenograms was $634.87, or 25 cents per student.

Journal of Pharmacology & Exper. Therap., Baltimore

74:1-98 (Jan.) 1942. **Partial Index**

Effects of Calcium Administered Parenterally to Normal and Parathyroidectomized Dog. P. L. Bedinger, A. B. Kendrick and R. W. Keeton, Chicago.—p. 1.
Studies on Toxicity of Actinomycin. H. J. Robinson, Rahway, N. J., and S. A. Waksman, New Brunswick, N. J.—p. 25.
Studies on Fate of Morphine. F. W. Oberst, Lexington, Ky.—p. 37.
Therapeutic Incompatibility Between Sulfapyridine and Quinine. B. K. Harned and Versa V. Cole, Philadelphia.—p. 42.
In Vitro Study on Synergistic Action of Sulfamido Compounds and Azochloramide on Various Pathogenic Micro-Organisms. E. Neter, Buffalo.—p. 52.
Effect of Treatment with Testosterone Propionate on Mercuric Chloride Poisoning in Rats. L. P. Longley, Cleveland.—p. 61.
Conjugation of Sulfanilamide by Pathologic Tissue in Vitro. A. Goth, Nashville, Tenn.—p. 71.
*Some Toxicologic and Pharmacologic Properties of Gramicidin, Tyrocidine and Tyrothricin. H. J. Robinson and H. Molitor, Rahway, N. J.—p. 75.
Experimental Comparison of Several Alkylmercuric Chlorides as "Skin Sterilizing" Agents. M. T. Bush and A. D. Bass, Nashville, Tenn.—p. 95.

Toxicologic and Pharmacologic Properties of Certain Antiseptics.—Robinson and Molitor present data on the acute and cumulative toxicity and pharmacologic properties of gramicidin, tyrocidine and tyrothricin as observed in 1,200 Swiss mice and 210 albino rats after oral, intravenous and intraperitoneal administration. Gramicidin and tyrothricin were more toxic than tyrocidine when injected intravenously and intraperitoneally. The preparations were not toxic on single or repeated administration by mouth. The physical properties of gramicidin and tyrocidine limit their application to infections in which local therapy can be employed; the absence of irritating properties in these agents gives them a definite advantage over other antiseptics and may extend the scope of their application. Although the toxicity of gramicidin and tyrothricin is greater than that of most agents of the sulfonamide group, their extraordinary bacteriostatic activity affords a large margin of safety. Pharmacologically and toxicologically the compounds have no pronounced specific properties. They do not have a definite specific effect on the respiratory or circulatory systems. Large single doses are usually tolerated without any definite effect, while multiple small doses cause a fall of blood pressure and impair respiration. With lethal doses the respiration stops shortly before the heart does. When these compounds are used clinically, care must be taken if rapid and direct absorption into the blood stream is likely.

Medical Annals of District of Columbia, Washington

10:459-500 (Dec.) 1941

Practical Points in Diagnosis and Treatment of Epilepsy and Migraine. W. G. Lennox, Boston.—p. 459.
Problems Arising in Chemotherapy of Pneumonia and Meningitis. H. F. Dowling, Washington.—p. 463.
Clinical Factors in Male Sterility Based on Study of 100 Cases. N. Belt, Washington.—p. 468.
Treatment of Fibrositis with Vitamin E. D. W. Ingham, Washington.—p. 470.
Ocular Emergencies in General Medical Practice. F. D. Costenbader, Washington.—p. 472.

New England Journal of Medicine, Boston

225:963-994 (Dec. 18) 1941

*Hiatus Esophageal Hernia, with Special Reference to Comparison of Its Symptoms with Those of Angina Pectoris. C. M. Jones, Boston.—p. 963.
The Doctor of One Hundred and Fifty Years Ago. H. H. Amsden, Concord, N. H.—p. 972.
Insulin Resistance in Case of Diabetes Mellitus and Chronic Lymphatic Leukemia: Report of Case. J. E. Levi and H. T. Friedman, Baltimore.—p. 975.
Leukemia: Agranulocytosis. H. Jackson Jr., Boston.—p. 978.

Esophageal Hernia.—Jones reviews symptoms presented by 91 patients with small and 37 with large hiatus hernia. The average age of the patients was 55, and most were overweight. A diagnosis was made of heart disease in 13 and of disease of the biliary tract in 22. Substernal pain was experienced by more than one third of the patients with a small but by only 5 of those with a large hernia. Pain in the shoulder, usually on the left, was noticed by about one fourth of all the patients. The pain of 8 of the patients with a small and of 4 with a large hernia radiated to the arm, and pain in the hand and fingers was complained of by 5 of the 8. Palpitation was noted by 6 patients with a small and by 4 with a large hernia. Dyspnea was noticed, respectively, by one tenth and by one third of the patients. Epigastric pain occurred in two thirds of 78 hospital patients and in 19 of 45 private patients. Pain in the costal margin on the right and/or the left side was present in 21 of the 91 patients and in 11 of the 37. About one fourth of the patients complained of pain in the back, and 4 patients with small hernias experienced pain directly under the left or the right scapula. Two of the latter had disease of the gallbladder. Axillary pain was noticed by 3 patients with a small hernia and difficulty in swallowing by 4. Heartburn was a characteristic symptom of small hernia in 14 private patients but in only 2 ward patients. Pain in the right side of the chest, shoulder or arm was observed by 13 patients with a small and by 6 with a large hernia. Eight of 25 patients with substernal pain, 4 of those with pain radiating to the shoulder and 3 of those with pain radiating to the arm stated that exertion frequently initiated the symptom. Nervous tension and acute emotional disturbances initiated symptoms suggesting angina pectoris. The intake of food was responsible for initiating substernal pain in 15 of 25 patients and in half of the patients complaining of pain radiating to the shoulder, arm or fingers. Only 11 patients had heart disease that may have contributed to the presenting symptoms. Study suggests that the pain in hiatus hernia is probably mediated over visceral afferent fibers supplying the esophagus and the cardiac or fundic portion of the stomach, or over the sensory afferent fibers from the diaphragm contained in the phrenic or middle or lower thoracic nerves. Overdistention of the esophagus or the herniated portion of the stomach may thus be responsible for anginal pain in any or all of its components. Treatment is essentially medical. Phrenicectomy or surgical repair is justified only for large hernias or when

medical measures fail. Acute symptoms are frequently helped by administration of glyceryl trinitrate. Assuming an upright or a semiupright position after eating is desirable. Adequate physical and emotional rest, sedation when needed and the avoidance of exercise shortly after the intake of food are valuable measures. Accompanying coronary disease and cholelithiasis should be properly evaluated.

Rhode Island Medical Journal, Providence

24:217-232 (Dec.) 1941

Henry Turner of Newport: Belated Tribute to Pioneer in Field of Cerebral Decompression. W. Pickles, Providence.—p. 217.
Torula Meningoencephalitis: Report of Case. I. C. Nichols, Wickford. —p. 221.
Ovarian Pregnancy: Case Report. P. S. Geller, Newport.—p. 223.
Needs of the Cardiac Child. H. E. Utter, Providence.—p. 225.

Southwestern Medicine, El Paso, Texas

25:381-414 (Dec.) 1941

Respiratory Tract Obstruction and Its Secondary Effects. T. C. Galloway, Evanston, Ill.—p. 381.
Recent Advances in Cancer. E. P. Palmer, Phoenix, Ariz.—p. 385.
Management of Chronic Arthritis. R. M. Smith, Dallas, Texas.—p. 393.
Cutaneous Complications in Treatment of Syphilis. H. D. Newton, San Diego, Calif.—p. 395.
Effect of Electromagnetic Radiations on Flocculation Tests for Syphilis. E. L. Breazeale, Tucson, Ariz.—p. 398.

Surgery, St. Louis

11:1-168 (Jan.) 1942

Effect of Bile Salts on Recovery of Liver Function After Release of Common Duct Obstruction. A. L. Berman, E. Snapp and A. C. Ivy, Chicago.—p. 1.
Blood Studies During Anesthesia: Reference to Infections and Noninfections. J. D. Martin Jr. and R. Robertson, Atlanta, Ga.—p. 11.
*Dynamic Changes in Experimental Pulmonary Embolism. R. S. Megibow, L. N. Katz and F. S. Steinitz, Chicago.—p. 19.
Reduction of Supracondylar Fracture in Children. V. L. Hart, Minneapolis.—p. 33.
Influence of Hypoproteinemia on Formation of Callus in Experimental Fracture. J. E. Rhoads and W. Kasinskas, Philadelphia.—p. 38.
Secondary or Postoperative Parotitis. G. F. Madding and R. E. Fricke, Rochester, Minn.—p. 45.
Influence of Caloric Restriction on Incidence of Spontaneous Mammary Carcinoma in Mice. M. B. Visscher, Zelda B. Ball, R. H. Barnes and I. Sivertsen, Minneapolis.—p. 48.
Experimental Studies on Alimentary Azotemia: III. Site of Blood Absorption. C. F. Chunn, Vicksburg, Miss.; H. N. Harkins and R. T. Boals, Detroit.—p. 56.
Pilonidal Sinuses Occurring over Higher Spinal Segments: Report of Case Involving Spinal Cord. H. P. Kooistra, Grand Rapids, Mich. —p. 63.
*Fusospirochetal Onychia and Paronychia. T. Benedek, Chicago.—p. 75.
*Malignant Meningiomas: Clinical and Pathologic Study. O. A. Turner, W. M. Craig and J. W. Kernohan, Rochester, Minn.—p. 81.
*Thromboangiitis Obliterans: Clinical Observations and Arterial Blood Oxygen Studies During Treatment of Disease with Sodium Tetrathionate and Sodium Thiosulfate. F. V. Theis and M. R. Freeland, Chicago.—p. 101.

Experimental Pulmonary Embolism.—Megibow and his colleagues measured directly, after the experimental production of pulmonary embolisms in 14 normal anesthetized or unanesthetized dogs, the pulmonary and the systemic arterial pressure, the systemic venous pressure and the heart and respiratory rates. Major multiple minor pulmonary embolisms were followed by systolic and diastolic pulmonary hypertension. Changes in the systemic arterial pressure were not striking. The systemic venous pressure usually rose; it rarely fell or showed no change. Changes in heart rate were inconstant. Ventricular fibrillation occasionally appeared terminally in an animal. Rapid progressive respiration usually developed at the same time as or soon after pulmonary hypertension ensued. Most frequently progressive cyanosis accompanied the respiratory changes. The theory of reflex coronary vasoconstriction as a cause of "sudden death" is hardly supported by the experiments, since mechanical factors explain the possible changes in coronary circulation. Death in cases of pulmonary embolism appears to be due to a rapid or slow failure of the right side of the heart, as a result of obstruction to the pulmonary vessel. So-called hypokinetic circulatory failure is in reality rapid failure of the right side of the heart.

Fusospirochetal Onychia and Paronychia.—Benedek believes that his case of onychia and paronychia caused and sustained by fusospirochetal organisms for two years is the first to appear in American literature. The progress of the condition, without lymphangitis or lymphadenitis, was slow but definite. The local and intravenous administration of neoarsphenamine failed to produce a cure, but the surgical removal of the affected nails resulted in prompt healing.

Malignant Meningiomas.—Turner and his associates state that among 370 intracranial meningeal tumors examined microscopically 36 showed definite malignant characteristics; 22 occurred in men and 14 in women. Twenty-two occurred during the third, fourth and fifth decades and the others around the ages of 8 and 60. The forms of the tumors were frequently bizarre and atypical. This, the authors suggest, is to be considered as progress of the anaplastic process beyond the stage of simple sarcomatous or malignant properties. The giant cells, seen frequently in the 14 more malignant tumors (11 occurred in male patients) were considered by Globus as evidence of vigorous cell growth. He believed that these cells establish a link between quiescent and malignant meningiomas. In many of the 22 low grade tumors or those with early malignant changes early or incomplete forms of giant cells were observed.

Thromboangiitis Obliterans.—Theis and Freeland report observations on studies of the arterial blood oxygen. Deficient oxygenation of the arterial blood was usually present in patients with thromboangiitis obliterans during the active stage of the disease. After two to six weeks of treatment the increase in the oxygenation of the arterial blood was accompanied by clinical improvement and in some cases by recovery (five years). The deficient oxygenation in most of the patients was affected by smoking. Prior to 1937 only sodium thiosulfate was available, but since then sodium tetrathionate (which is slower in action but more prolonged in its effect) has been used. For acutely affected persons, when an immediate effect was desirable injections of the thiosulfate were given every other day and the tetrathionate on the alternate days. As the acute stage subsided, biweekly or weekly injections of the sodium tetrathionate solution were given. The usual intravenous dose was 1 Gm. of sodium thiosulfate and 0.4 or 0.6 Gm. of sodium tetrathionate dissolved in 10 cc. of sterile distilled water. Transitory reactions may occur with either drug, but they are generally relieved by the drinking of a glass of water. No serious reaction occurred after almost 8,000 injections. The appearance of the blood and an occasional sedimentation test are usually sufficient to determine the course of the disease. Passive vascular exercise was used, with benefit, for deficient circulation due to thrombotic occlusion of the peripheral arteries. For patients who have recovered completely all treatment may be discontinued, but when smoking is resumed periodic injections should be continued.

West Virginia Medical Journal, Charleston

38:1-48 (Jan.) 1942

Public Health Administration. R. H. Riley, Baltimore.—p. 1.
Diagnosis and Treatment of Cardiac Emergencies. W. Dressler, New York.—p. 9.
*Sulfaguanidine in Treatment of "Bloody Flux." G. M. Lyon, T. G. Folsom, W. J. Parsons and Irma Sprouse, Huntington.—p. 19.
Sinusitis with Subsequent Meningitis. E. C. Hartman, G. Geyerhahn and S. A. Solomon, Parkersburg.—p. 27.
Resurvey on 243 Cases of Anterior Poliomyelitis in West Virginia: Report. A. M. Price and Ester M. Finley, Charleston.—p. 29.
Leukorrhea: Its Significance and Treatment. J. A. Hepp, Pittsburgh. —p. 32.

Sulfaguanidine for "Bloody Flux."—Lyon and his associates present data on 259 patients who had "bloody flux" and were treated with sulfaguanidine. The drug has proved to be quickly effective and safe for the treatment of such patients in the home, the office and the hospital. They recommend an initial dose of 0.1 Gm. of sulfaguanidine per kilogram of body weight and thereafter one of 0.05 Gm. per kilogram of body weight every four hours for three days and then the same dose every eight hours for two days. If the patient has not recovered by this time and the character of the stool has not changed they advise treatment with sulfathiazole for five days. Sulfaguanidine, because of its freedom from toxic effects, is preferred to sulfathiazole. Its greater safety is not to be overlooked when treatment must be given in the home. The frequency of failures, relapses, second infections and chronic intestinal indigestion has been greatly lowered by sulfaguanidine therapy.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Medical Journal, London

2:759-794 (Nov. 29) 1941

*Combined Active and Passive Immunization Against Diphtheria: II. Control of Epidemics in the Field. F. Fulton, A. Q. Wells, Joan Taylor and C. S. Wilson.—p. 759.
Industrial Medical Services in Great Britain: Critical Survey. D. Stewart.—p. 762.
"Ether Convulsions." H. J. Brennan.—p. 765.
Encopresis (Incontinence of Feces) in Children. C. Burns.—p. 767.
Macrocytic Anemia Following Gastroenterostomy. N. S. Gordon and J. Japa.—p. 769.
Geographic Distribution of Gastric and Duodenal Ulcers in British Isles, with Notes on Etiology of Peptic Ulcer. B. M. Nicol.—p. 780.

Immunization Against Diphtheria.—Fulton and his co-workers attempted to prevent the spread of diphtheria in a closed or semiclosed community by detecting all carriers and segregating them until the remaining persons acquired an adequate active immunity. They adopted the following method when an outbreak was evident in a school: 1. Swabs taken from the nose and throat of every child and teacher in nonresidential schools and of every person in residential schools were cultured on tellurite blood agar, and diphtheria bacilli were typed. All strains were tested for virulence to guinea pigs. 2. At the same visit all children were given subcutaneous injections of 0.1 cc. of alum precipitated toxoid into the left arm and 350 to 500 units of refined diphtheria antitoxin globulin into the right arm. 3. All carriers were isolated or segregated when the results of the swab culture were known. 4. Four weeks later all children, including the carriers, were given 0.3 cc. of alum precipitated toxoid into the right arm. 5. All carriers were allowed to return to school two weeks after the second inoculation. They were permitted to mix freely, but in residential schools they were forbidden to participate in games with visiting teams. Any carrier from whom three consecutive swabs negative for diphtheria bacilli when cultured on tellurite blood agar were obtained before the end of the six weeks of segregation was allowed to return to school. This technic was adopted in seven outbreaks of diphtheria. The population at risk was about fifteen hundred. Each outbreak ceased immediately. Only 5 new infections occurred after the first combined injection. The method protects the children at once, and the closing of schools becomes unnecessary.

2:795-836 (Dec. 6) 1941

Observations on Some Normal and Injurious Effects of Cold on Skin and Underlying Tissues: I. Reactions to Cold and Injury of Normal Skin. T. Lewis.—p. 795.
Failure of In Vitro Tests as Guide to Value of Stored Blood. P. L. Mollison and I. Maureen Young.—p. 797.
*"Wound Phagedena": Report of Two Cases. A. Callam and A. Duff.—p. 801.
Enuresis in Adolescents. R. C. Browne and A. Ford-Smith.—p. 803.
Combined Intrauterine and Extrauterine Pregnancy: Case. R. B. Leech.—p. 805.
Unusual Reticulocytosis in Untreated Case of Pernicious Anemia. W. T. Cooke.—p. 806.

"Wound Phagedena."—Callam and Duff report 2 cases of a spreading infection of the skin and subcutaneous tissue which arose from an infected wound or sinus. The condition appeared to be one manifestation of a clinical entity, such as postoperative cutaneous gangrene and similar conditions, closely related to the "phagedena" of former times. The infecting agent was an anaerobic streptococcus associated with Proteus vulgaris. The condition was so rapidly progressive in 1 case as to be almost inevitably fatal, death occurring on the twenty-first postoperative day. Cure was effected in the other case by wide excision of the lesion.

Lancet, London

2:689-718 (Dec. 6) 1941

*Frostbite and Kindred Ills. R. Greene.—p. 689.
*Response to Vitamin K: Liver Function Test. R. Kark and A. W. Souter.—p. 693.
Preservation of Liquid Complement Serum. G. M. Richardson.—p. 696.
Mammary Carcinoma: Response to Implantation of Male Hormone and Progesterone. A. A. Loeser.—p. 698.

Frostbite.—Greene states that the conditions of the present war have produced two disorders, immersion foot and shelter foot, and that these are closely related to frostbite and to trench foot. Shelter foot was often seen among shelter dwellers in London in 1940 and 1941 who sat up all night without compensating rest in a horizontal position during the day. Immersion foot was encountered in persons who, after a shipwreck, spent a long time in waterlogged boats. In shelter foot the swelling of the feet is painless at first. After a while the swelling extends up the leg. The condition did not arise in wardens who, though exposed to the same degree of cold and damp, were frequently on their feet. The wooden bars of the deck chairs used by most of the patients exerted prolonged pressure on the popliteal fossa, causing venous stagnation and increased capillary permeability. Immersion foot is almost identical with trench foot, and its causes are the same; cold, heat after cold, dampness, venous stagnation, wind, anoxia, nutritional deficiency and trauma all may play a part. In true frostbite the immediate cause is cold, frequently aggravated by wind and anoxia. In trench foot and immersion foot dampness, associated with cold and venous stagnation, is probably the most important factor. Though the four conditions have causes which vary in relative importance they act through a common channel —transudation from damaged blood vessels. One can usually prevent them by bearing in mind their causes. Treatment depends on the stage at which it is undertaken. The premonitory symptom of frostbite of the face may be a white patch, which can be cured by the application for a few seconds of a warm ungloved hand. If the foot or the hand becomes numb, the boot and sock or glove must be removed and the limb warmed by placing it inside another man's clothing. Rubbing the affected parts is extremely dangerous. If the tissues are dead they are beyond care, but if they are alive warmth, never greater than that of the human body, will quickly restore circulation. If these measures fail, the affected part should be cleansed gently, painted with an active antiseptic (proflavine), wrapped in sterile dressings and in many layers of wool and rested. Antitetanus serum, hot food and drinks, extra clothing, comparative warmth and security and, if the frostbite has occurred above sea level, pure oxygen are indicated. Thereafter, a policy of inactivity should be pursued unless sepsis develops, when it should be treated like sepsis from any other cause. Amputation, without sepsis, is seldom necessary and never urgent. It may be advisable later for esthetic or orthopedic reasons, but the question should be left to the judgment of a surgeon working amid the conveniences of a hospital at home.

Response to Vitamin K.—According to Kark and Souter, of 200 patients suspected of having hypoprothrombinemia the clinical diagnosis in 51 was portal and biliary cirrhosis, catarrhal jaundice, toxic or infectious hepatitis and intense jaundice. In assessing the type and extent of the hepatic disorder in these patients the authors determined the initial level of the blood prothrombin and its character and degree of response after the administration of vitamin K. There were five types of response. In patients with intense jaundice the low blood prothrombin level returned to normal quickly after vitamin K therapy. This favors a diagnosis of obstructive jaundice. Patients with gross hepatic disease failed to respond to vitamin K therapy. Apparently when the blood prothrombin concentration is less than 30 to 35 per cent of normal, advanced hepatic failure is probable. This is a grave prognostic sign. Patients with a lowered blood prothrombin level which rose somewhat but remained fixed at a subnormal level despite repeated administration of vitamin K had acute or subacute parenchymatous hepatic damage of a moderate and variable degree. For patients in whom the blood prothrombin level gradually rose with treatment, coincident with clinical improvement, the diagnosis was infective cholangitis, catarrhal jaundice, acute or toxic hepatosis or obstructive jaundice complicated by an infective process. When the prothrombin level fluctuated at a subnormal level which was above the threshold for hemorrhage, irrespective of therapy, the patients had chronic and long-standing hepatic disease, usually unassociated with jaundice. For patients with hepatic disease who responded incompletely or not at all to vitamin K therapy, transfusion of fresh blood or fresh plasma was the only therapeutic measure that increased the prothrombin concentration of the blood. Such transfusion should be employed, before and after operation, if any surgical procedure is necessary.

Ophthalmologica, Basel

102:193-256 (Oct.) 1941. **Partial Index**

Photographic Determination of Depth and Volume of Anterior Chamber of Human Eye. M. Heim.—p. 193.
Cicatricial Shrinkage of Conjunctiva as Industrial Lesion in Dyers. R. Brückner.—p. 221.
Senile Changes in Eye. F. P. Fischer.—p. 226.

Cicatricial Shrinkage of Conjunctiva in Dyers.—Brückner describes bilateral cicatricial shrinkage of the conjunctiva in 2 aged men who for several decades had worked in dyeing and cleaning establishments. The development of the cicatricial changes had apparently been very gradual. Both men denied direct corrosion by chemicals or a severe conjunctivitis. Trachoma could likewise be excluded. The disorder is apparently benign in contradistinction to the disorders of the pemphigus group and to the "essential" conjunctival shrinkage. The condition differs in pathogenesis and course from all hitherto described disorders with similar ophthalmologic symptoms. The author mentions some of the chemicals used in dyeing establishments, such as sulfuric acid, hydrochloric acid, acetic acid, formic acid, chlorine, ammonia, chrome, sulfur, aniline dyes and potassium cyanide, and suggests that some of these substances may be present in the form of gas or steam, either pure or in a chemical combination, in the air of dyeing establishments. They may be present in such a low concentration as not to cause any particular annoyance, but they may come in contact with the conjunctiva either directly or mixed with the lacrimal fluid. They may thus injure the epithelium and probably the subepithelial tissue. In view of the rarity of the condition, the author suggests that individual predisposing factors, such as metabolic changes in the subconjunctival tissues during the physiologic involution of senescence, may play a part.

Arch. Arg. Enf. d. Ap. Res. y Tuberc., Buenos Aires

9:283-334 (Oct.-Nov.) 1941. **Partial Index**

*Bronchocinematography: Its Application to Study of Dynamics of Bronchi. M. R. Castex, E. S. Mazzei and M. Malenchini.—p. 307.

Bronchocinematography—Castex and his collaborators state that there are no reports in the literature on the performance of bronchography by means of roentgen cinematography. They used Abreu's technic, in which a camera with an objective opening which varies within 1 : 1.4 and 1 : 0.85, a tension of 100 kilowatts, an intensity within 50 and 100 milliamperes and a tube of 10 kilowatts or a rotatory anode of 20 or 40 kilowatts are used. By this technic the changes of the bronchi during the consecutive phases of every respiratory cycle can be photographed. The films can be projected on the screen with normal or retarded speed. The functioning time of the apparatus is twelve seconds when 50 milliamperes and 100 kilowatts are used and 5 seconds when 100 milliamperes and 100 kilowatts are used. Any good photographic emulsion can be used. The roentgen cinematographic results confirmed previous observations of the authors in which they found that normal bronchi have two types of respiratory movement. Passive movements are pulsations from the heart, the aorta and the pulmonary artery and also from the esophagus during deglutition. Active movements include changes in the length and caliber of the bronchi, peristalsis, undulation and torsion. The normal bronchi are elongated and dilated during inspiration and shortened and narrowed during expiration. They exhibit inspiratory movements for fanwise dispersion of air toward the alveoli and movements of torsion near the lower lobes and of retraction during expiration. The inspiratory changes of the caliber of normal bronchi or of bronchi in a pathologic state are visible during roentgen cinematography. In cases of chronic bronchitis the caliber of the bronchi either does not increase during inspiration or increases but little. The degree of impaired bronchial dilatation depends on the more or less acute local inflammation. In bronchiectasis the caliber of the bronchi either does not increase or it diminishes during inspiratory elongation of the bronchi. In cases of bronchial asthma the bronchocinematographic picture is difficult to interpret. The particular changes in these cases are due to forced respiration in the presence of hypertonicity of the bronchopulmonary myoelastic system. In Ayerza's disease the bronchial changes are predominantly of the type of chronic bronchitis, and to a lesser degree of the type observed in bronchial asthma.

Archivos Argentinos de Pediatría, Buenos Aires

16:435-546 (Nov.) 1941. **Partial Index**

Postvaccinal Polyneuritis and Retinitis in Child Aged 6. J. P. Garrahan, J. J. Murtagh and J. C. Traversaro.—p. 435.
Leukemia with Embryonal Cells Probably of Congenital Origin. M. Acuña and Maria Teresa Vallino.—p. 443.
Prognostic Value of Different Elements in Whooping Cough Bronchopneumonia. F. Bazán, R. Maggi and E. Sujoy.—p. 449.
*Sulfaguanidine in Diarrheas of Infants and Young Children. F. J. Menchaca.—p. 473.
Comparative Study of Mantoux Reaction with Human and Bovine Tuberculin. F. Escardo and R. Rabanaque Caballero.—p. 489.

Sulfaguanidine in Diarrheas of Children.—Menchaca reviews the literature on diarrhea of infants. Marshall and his collaborators at Johns Hopkins found a series of chemical compounds with intense antibacterial power in the intestinal contents. Of these sulfaguanidine appeared to be most efficacious. The author reports the histories of 20 infants and children from 3 months to 6 years of age in whom sulfaguanidine was used to counteract diarrhea. The favorable results obtained justify its further use.

Boletín de la Soc. de Obst. y Ginec., Buenos Aires

20:643-678 (Dec. 10) 1941. **Partial Index**

*Magnesium Sulfate in Hyperemesis of Pregnancy. D. E. Nölting and R. Caso.—p. 670.

Magnesium Sulfate in Hyperemesis in Pregnancy.—Nölting and Caso treated 50 pregnant women with acute and subacute vomiting by intravenous injections of 1 or 2 cc. of a 50 per cent magnesium sulfate solution in 10 or 20 cc. of physiologic solution of sodium chloride. The patients were in the first three months of pregnancy. The previous treatment, by providing rest to the stomach, administration of sedatives, intravenous or subcutaneous injection of dextrose solution and of physiologic solution of sodium chloride, and the administration of insulin and liver extract were of no avail. Seven patients in the group of 22 multigravidas had previously had therapeutic abortion because of acute vomiting. The injections were administered slowly. They were given twice a day, thirty minutes before breakfast and supper, for ten or fifteen consecutive days. An abundant diet with solid food and fruit juices was given. Patients with dehydration and moderate hepatic insufficiency were given subcutaneous injections of dextrose and physiologic solution of sodium chloride, insulin and liver extracts. Vomiting was controlled early in the course of the treatment in 32 cases. In 18 in which vomiting diminished but was not controlled within ten days two daily intramuscular injections of 5 cc. of a 15 per cent magnesium sulfate solution were administered, one an hour before breakfast and the other an hour before supper, for ten more days. All the patients were cured and were able to tolerate pregnancy up to term. The treatment is harmless, well tolerated and effective. Failing heart constitutes the sole contraindication.

Día Médico, Buenos Aires

13:793-820 (Aug. 11) 1941. **Partial Index**

*Magnesium Sulfate in Seasickness. José Maris Poch.—p. 798.

Magnesium Sulfate for Seasickness.—Poch injected intramuscularly a solution consisting of 1.25 Gm. of magnesium sulfate, 0.05 Gm. of caffeine and 0.25 mg. of atropine. The injections were given at intervals of twelve hours. As a rule two injections were sufficient; in rare instances a third injection was required. The observations were made on healthy sailors subject to a severe form of seasickness. The symptoms consisted of nausea, vomiting, profuse sweating, bradycardia, frontal headache, with or without photophobia, and a fall in the arterial blood pressure. The symptoms greatly diminished within the first four hours after the first injection and were controlled by the second injection. In a few cases in which nausea persisted it was controlled by the third injection. Arterial blood pressure promptly returned to normal. The patients were able to continue at work. There was no recurrence. The injection produced a moderate amount of pain, which lasted for several hours.

Revista Brasileira de Biologia, Rio de Janeiro

1:365-474 (Dec.) 1941. **Partial Index**

*Histoplasmosis in Child: Case. E. Villela and Madureira Pará.—p. 449.

Histoplasmosis in Child.—The case reported by Villela and Madureira Pará is the thirteenth in the medical literature, the fifth of the disease in a child and the first in Brazil. The disease is probably more frequent than is believed. It may be mistaken for visceral leishmaniasis, particularly in regions where that disease is endemic. The disease is fatal. The authors' patient, a boy aged 3 years, lived in unhygienic conditions among dogs and cats. He presented fever and progressive debility for one month. Later there developed diarrhea with blood in the feces and progressive emaciation. The treatment consisted in administering polyvalent antidysenteric vaccines and vitamins A and D. Jaundice and red spots over the body appeared one week before death. The diagnosis was made from the microscopic study of the liver, which was enlarged, waxy in color and friable. The microscopic appearance was typical of histoplasmosis. The parenchyma of the liver presented enormous proliferation of reticuloendothelial cells, which were engorged with Histoplasma capsulatum. The monocytic cells were also increased and contained histoplasma. Identification of H. capsulatum and its differentiation from leishmania in human tissues is best accomplished by the use of Heidenhain's iron hematoxylin stain, the Giemsa, Gram and Goodpasture stains and the double impregnation method of Del Rio-Hortega. The rarity of histoplasmosis in Brazil may be seen from the fact that, of 186,000 cases in which liver specimens were examined microscopically in the laboratory of the Yellow Fever Service, in only 1 has this blastomycosis been found, while in 131 cases in the same series visceral leishmaniasis was discovered.

Revista Médica de Chile, Santiago

69:707-790 (Nov.) 1941. **Partial Index**

*Bite of Wheat Spider (Latrodectus Mactans). R. Gajardo Tobar.—p. 707.

*Treatment of Ringworm Infections of Scalp with Gonadal Substances. Yañez, Weinstein, Bravo and Guzmán.—p. 713.

Serologic Reactions of Syphilis and Their Interpretation in Cases of Venereal Lymphogranuloma. P. Chana Cariola.—p. 715.

Angioneuromatous Tumors. L. Marin Couchot and I. Mena.—p. 719.

Black Widow Spider Bites.—Gajardo Tobar describes observations in 23 cases of bite by the black widow spider, Latrodectus mactans, a species found throughout Western America from California to Patagonia. The spiders are most numerous during the dry months. Harvesters, stookers and threshers are most exposed. The bite produces a sensation of lancing, and if the cause is searched for the spider may be found in the clothing. The venom of Latrodectus mactans is neurotropic. The bite is followed by a ten minute latent period, after which the local pain recurs and rapidly increases to involve the entire body. Clonic contractions, tremors, spasmodic movements and convulsions follow. The symptoms and pains are intermittent and reach their maximum intensity in the waist, arms and legs. The muscular contractions and the excruciating pain bring about rigidity of the abdomen and of the chest. The patient experiences precordial and abdominal oppression and has the feeling of approaching death. There may be disorientation, hallucinations, delirium, debilitating sweats, profuse salivation and lacrimation. The sensitivity of the skin and the reflexes are exaggerated. The respirations are rapid and shallow. Temporary tachycardia is followed by bradycardia. The arterial pressure increases and later falls. Albuminuria and uremia develop. Intestinal and vesical paralysis develop, and the urinary secretion is diminished. There may be priapism, ejaculations and enuresis. After a few hours the symptoms abate somewhat, only to return in paroxysms. The disorder persists for a week. The convalescence is characterized by physical and mental fatigue. The literature reports fatal cases, but as a rule the patients recover. The bite confers a temporary immunity. In animals the immunization persists for about three months. Persons have been bitten by Latrodectus mactans several times and each time have had all the symptoms of poisoning. The treatment is chiefly symptomatic. Hot baths, morphine and atropine sulfate are employed to counteract pain, convulsions and spasms. Sparteine and camphor liniment are administered as cardiac stimulants. Physiologic solution of sodium chloride, dextrose solution and thiamine hydrochloride are given to counteract the intoxication. It would be most desirable to obtain a specific serum as recommended by Vellard and as prepared by Troise in Argentina. The difficulty in producing a specific serum is the insufficient quantity of venom available.

Gonadal Substances in Ringworm Infections of Scalp.—Yañez and his collaborators point out that ringworm infections of the scalp occurring chiefly in children of school age are more or less contagious, depending on the species of fungus. Infections with some species tend to spontaneous recovery after several months. A cure in one region may be accompanied by infection in another, so that the disorder continues for months or years. To obtain definite results it is necessary to resort to depilation of the scalp. With the exception of favus, ringworm infections of the scalp disappear spontaneously at puberty. This fact suggested the possibility of reproducing the puberal condition which favors elimination of the parasite by the use of estrogens. Yañez injected estrone into a menopausal woman with tinea tonsurans. The infection disappeared in the course of ten days after the administration of five doses of estrone. The authors administered gonadotropic substance to children with ringworm infections of the scalp. The lesions of tinea showed changes from the fourth or fifth day after the beginning of the treatment. The scales disappeared, the diseased hair fell out and the plaques cleared up. The cure was usually complete on the tenth or the twelfth day. There was no apparent difference in the employment of male or of female gonadotropic substance for persons of either sex. The treatment has been used for 34 children (25 boys and 9 girls); failure was recorded in the treatment of 3.

Revista Médica de Córdoba, Córdoba

29:609-650 (Nov.) 1941. **Partial Index**

*Lymphogranulomatosis Maligna During Childhood. A. A. Ferraris.—p. 609.

Pseudomiliary Colloidal Degeneration of Skin: Case. F. Strada and M. Rodeiro.—p. 621.

Lymphogranulomatosis Maligna in Childhood.—Ferraris believes that malignant lymphogranulomatosis is relatively frequent. Of every 4 boys with enlarged cervical lymph nodes 1 was found to have Hodgkin's disease. The author reports observations on 15 children, aged 5 to 12 years; 14 were boys and 1 a girl. Preponderance of the male sex has been observed by other investigators. The onset is generally insidious. There is a gradual enlargement of the cervical lymph nodes; the general condition is impaired; the child lacks appetite, is pale and at times has fever. In 70 per cent of the cases the author observed splenomegaly and in 60 per cent hepatomegaly. The Wassermann and Kahn reactions were negative in all. The Mantoux reaction was positive in only 2 cases; this incidence was approximately that seen in healthy children. The results of Gordon's test at times contradicted the results of the microscopic examination of the nodes. Sternal puncture likewise proved unreliable. Biopsy of an involved node is the most reliable diagnostic method. The treatment consisted in fractional roentgen irradiation; in some cases of late disease sulfonamide derivatives were given. The disease always terminated fatally in one to five years.

Revista Médica de Rosario, Rosario de Santa Fe

31:1069-1182 (Nov.) 1941. **Partial Index**

Effects of Digitalis on Electrocardiogram and Its Clinical Significance. C. Alvarez and A. Delle Vedove.—p. 1069.

*Early Diagnosis of Cancer of Breast. J. Benzadón.—p. 1098.

Spontaneous Hemopneumothorax. A. B. Arroyo.—p. 1119.

*Treatment of Mercurial and Bismuth Stomatitis by Ascorbic Acid. J. V. Marín.—p. 1127.

Benign Lymphocytic Meningitis. L. Levit, E. S. Weiler and J. Luppi.—p. 1135.

Early Diagnosis of Cancer of Breast.—A hard, woody painless tumor whose borders are vaguely defined, suggests, according to Benzadón, a malignant degeneration of a benign tumor. The hard, woody consistency, which does not permit folding while one picks the tissue up between the hands, is characteristic of malignant growth. Retraction of the nipple may appear later than the aforementioned signs; its presence in

a tumor which shows no signs of inflammation confirms the suspicion of malignancy. Pinching of the skin over a tumor may reveal adhesion to the skin otherwise not observed. This fold test indicates that the neoplasm is malignant. Walther's sign or the wrinkle sign has the same significance. A positive Halsted sign is of great value. A black spot of inklike shadow with irregular outlines on transillumination suggests a malignant tumor. Pneumomastic roentgenoscopy (introduction of air, oxygen or carbon dioxide before roentgenoscopy) can aid in the early diagnosis by revealing a shadow more opaque than the gland with indistinct outlines and at times with diminution of one of the clear spaces. Mammography with the injection of a contrast medium in cases of malignant tumors is not innocuous. Punch biopsy with the finding of malignant cells confirms the diagnosis. A negative biopsy does not establish the diagnosis. Punch biopsy may be valuable in differentiating a solid from a liquid tumor and a neoplasm from a chronic suppurative process. The author does not recommend biopsy; he prefers a complete extirpation of the tumor and a microscopic examination. Early diagnosis is possible, provided the patient consults a physician early enough.

Ascorbic Acid in Mercurial and Bismuth Stomatitis.—Marín observed mercurial and bismuth stomatitis among syphilitic patients. Absence of ascorbic acid from their blood and urine suggested the advisability of administering the acid. His experience with ascorbic acid therapy in 10 cases of syphilis suggests that the acid has a detoxicating effect on the mercurial salts probably because of its reducing action. Ascorbic acid cures mercurial and bismuth stomatitis. It permits continuation of serial mercury and bismuth therapy for patients who do not tolerate compounds of these metals. Injection of large doses of ascorbic acid produces rapid, optimal results; its oral administration is not effective.

Revista Med. Soc. de Sanidad y Benef. Municip., Havana

1:79-158 (Oct.-Dec.) 1941. **Partial Index**

*Whooping Cough in Havana: Preventive Vaccination. A. Argudín García.—p. 103.

Vaccination in Whooping Cough.—Argudín García, head of the Municipal Department of Infant Hygiene of Havana, administered vaccines against whooping cough to 1,556 infants who were observed in the department from January to July 1941. The vaccine used was prepared with pure pertussis antigen. It was administered subcutaneously in doses of 0.25, 0.5, 0.75 and 1 cc., with intervals of three days. No untoward reactions occurred. In a large number of children the hemogram after vaccination changed to that of the type of whooping cough, showing acquired immunity. Whooping cough developed in only 5 per cent of the vaccinated children, and it was attenuated. The morbidity and mortality diminished.

Zentralblatt für Chirurgie, Leipzig

68:1473-1576 (Aug. 9) 1941. **Partial Index**

Treatment of Uncomplicated Fracture Luxations in Ankle Joint. A. Buzello.—p. 1485.
Histologic Aspects of Meniscus After Accidental Injuries. W. Ceelen. —p. 1491.
*Involvement of Arteries in Intermittent Claudication of Arm: Treatment by Periarterial Sympathectomy. K. Ebhardt.—p. 1499.
Fenestrated Plaster Bandages and Hoop Bandages. J. C. Lehmann. —p. 1516.
Experiences with Close Range Roentgen Irradiation According to Chaoul. H. Schneider.—p. 1519.
*Etiology and Therapy of Tendovaginal Panaritium. E. R. Welcker. —p. 1564.

Periarterial Sympathectomy for Intermittent Claudication.—Ebhardt reports that a youth aged 19 sustained a fracture of the radius, which was treated with a cast and which healed in a good position. A swelling of the arm remained, and movement of the wrist joint was slightly impaired. Several months later attacks developed during which the hand and arm became blue, cold and insensitive. A thrombotic closure of the axillary vein was considered, but, since the symptoms responded to conservative measures, intervention appeared unnecessary. Two years after the fracture, while swimming, the patient suddenly had a circulatory disturbance in the arm. The member became cold, cyanotic, insensitive and painful. The attack lasted for half an hour. Considerable exacerbation of symptoms took place. An operation disclosed that the disorder was the result not of venous thrombosis but of a spasm of the vessels which resulted from a chronic induration of the axillary connective tissue. Freeing of the artery failed to improve the circulation. A periarterial sympathectomy was successful in ameliorating the condition. The author does not consider sympathectomy as the procedure of choice for the treatment of intermittent claudication but believes that it is advisable only for some particularly constituted patients.

Tendovaginal Panaritium.—According to Welcker, clinical observation and bacteriologic studies demonstrated the etiologic significance of the subcutaneous panaritium in the development of the tendovaginal abscess. Early and correct surgical treatment of the subcutaneous panaritium is the best prophylactic measure against the involvement of the tendon. Simple opening of the proximal end of the tendon sheath (modification of Iselin's method) as treatment of tendovaginal suppuration of the second and fourth fingers with suspension of the splinted arm produced surprisingly favorable results in cases in which the tendon itself had not become involved. The results of this intervention were especially favorable in regard to functional restoration.

Nordisk Medicin, Stockholm

12:3227-3306 (Nov. 15) 1941. **Partial Index**

Hospitalstidende

*Adult or Idiopathic Myxedema and So-Called Benign Hypothyrosis. E. Jarløv.—p. 3237.
Passage of Sulfonamide Derivatives from Blood to Spinal Fluid. P. Bechgaard, E. Lohse and E. Vermehren.—p. 3247.
Artificial Changes of Cerebrospinal Fluid (Apart from Admixture of Blood) During Evacuation of Larger Amounts of Cerebrospinal Fluid with Simultaneous Insufflation of Air. E. Lund and A. V. Neel. —p. 3249.

Adult or Idiopathic Myxedema and So-Called Benign Hypothyrosis.—Jarløv compares classic myxedema (British Myxedema Commission) and benign hypothyrosis (Hertoghe) and reports 78 cases of so-called hypothyrosis. He concludes that clearcut myxedema is rare. Certain symptoms which must be regarded as symptoms of classic myxedema occur in as many patients with normal basal metabolic rate as in patients with a lowered rate. This is true of the myxedematous habitus, which occurred in only 1 of 7 younger patients and in 4 of 8 older patients with a lowered rate and in 6 of 29 younger patients and in 8 of 17 older patients with a normal rate. Impairment of memory, edema, dryness of the skin, loss of hair, brittleness of the nails, oliguria and amenorrhea were relatively infrequent symptoms. Dryness of the skin affected the younger patients with a normal rate more than any other group. Nervousness and headache were relatively frequent. Constipation and adiposity occurred in more of the groups with a normal rate than in those with a lowered rate. The sensation of cold played a relatively important part in the groups with a lowered rate, but in all the groups it responded well to treatment with thyroid, as did also the tired feeling, important in all groups but wholly absent in some patients with otherwise typical myxedema. The author asserts that adiposity does not play the part in hypothyrotic symptoms formerly ascribed to it. There were relatively many patients with a normal basal metabolic rate and symptoms like those of classic myxedema who reacted so favorably to thyroid therapy that they must be assumed to have had a thyroid deficiency. A lowered rate must therefore be regarded as a symptom coordinated with the other symptoms. In the material all transitions were represented from cases with the symptoms of classic myxedema to cases characterized by only one or a few of these symptoms. Certain cases of asthenia and of stubborn constipation, cases interpreted as of muscular rheumatism, some cases of edema and some others were included. Neither the symptoms named nor the lowered metabolic rate can determine the indications for thyroid therapy or the dose; only the reaction to the substance in each case can be applied as the criterion. He suggests that with the present status of knowledge the designation hypothyrosis be maintained for a number of pathologic conditions having certain common features and forming an indefinitely limited group which can be divided into two indefinitely limited subgroups, malignant and benign hypothyrosis.

Book Notices

Subacute Bacterial Endocarditis. By Emanuel Libman, M.D., Consulting Physician, the Mount Sinai Hospital, New York City, and Charles K. Friedberg, Adjunct Physician, the Mount Sinai Hospital. Edited by Henry A. Christian, A.M., M.D., LL.D. (Reprinted from Oxford Loose-Leaf Medicine.) Cloth. Price, $2.75. Pp. 108, with 19 illustrations. New York, Toronto & London: Oxford University Press, 1941.

This excellent summary of subacute bacterial endocarditis is based in large part on Libman's own long experience with the disease. He writes, for example, that between 1899 and 1930 he had observed at least 1,000 cases. The book is subdivided into sections on definition and classification of endocarditis, classification of bacterial endocarditis, the various aspects of subacute bacterial endocarditis including etiology and pathogenesis, pathology, clinical features, diagnosis, cases of mild subacute bacterial endocarditis, bacteria free stage of the disease, transitional endocarditis, recurrent endocarditis, prognosis, cause of death, prophylaxis and treatment. There is a bibliography of one hundred and ninety-eight references.

There are many pertinent observations concisely made, a few examples of which in the first fifteen pages are:

Bacterial endocarditis is subdivided into acute and subacute bacterial endocarditis. As implied in the terminology, these subdivisions are based on the duration of the disease, the acute form including cases with a course of, in general, less than six weeks, and the subacute, cases with a course of more than six weeks. This differentiation, however, is not an arbitrary one except in certain borderline cases. The two forms of bacterial endocarditis are, as a rule, sharply distinguishable both as to their causative agents and as to their clinical and pathological features. The acute cases are due almost always to pyogenic organisms, while the subacute cases are caused by organisms of relatively low virulence.

Bacterial endocarditis is a terminal or terminating complication in about 10 to 20 per cent of cases of rheumatic heart disease . . . Subacute bacterial endocarditis occurs much more frequently than acute bacterial endocarditis. In over 90 per cent of the cases the causative organisms are nonhemolytic streptococci, usually the alpha (viridans) and occasionally of the gamma (anhemolyticus) variety.

Subacute bacterial endocarditis may appear in the presence of a mixed infection. The most common combination is an endocarditis due to nonhemolytic streptococci with a secondary pneumococcus bacteremia, usually secondary to a lobar pneumonia. We have observed also a secondary implantation of Staphylococcus aureus on valvular vegetations due to nonhemolytic streptococci.

Agonal and postmortem blood cultures usually are unreliable.

An adequate quantity of blood must be drawn, at least 20 cc., and a variety of media employed. Aerobic and anaerobic cultures should be made. Since the organisms may enter the blood stream from the vegetations only intermittently, it may be necessary to take repeated blood cultures in order to find the causative organism.

Blood cultures should be observed for a minimum of four days, but it is preferable to keep them routinely for eight to ten days. Sometimes it is advisable to observe the cultures even longer, for, especially after chemotherapy, such as with sulfanilamide or sulfapyridine, growth of the organisms may not be discovered until after two or three weeks. The blood cultures even may remain completely sterile as long as the patient is under treatment with these drugs while positive cultures are obtained subsequently, when they are stopped. Recently reported studies (Strauss, Lowell and Finland) indicate that by the employment of para-aminobenzoic acid, which inhibits sulfonamide action, it will be possible with such a negative result as is obtained to determine whether bacteria are really absent. This interesting substance has most effect against sulfanilamide, less against sulfapyridine and still less against sulfathiazole.

Usually the site of origin of the endocardial infection is not evident. Clinical observation leads us to the assumption that the portal of infection is, as a rule, about the teeth or in their roots, in the tonsils, in the accessory sinuses or in other parts of the upper respiratory tract.

The sites of localization of the bacterial endocarditis are determined chiefly by mechanical factors. There is evidence that bacteria settle and multiply wherever they are sprayed forcefully on a receptive area.

Active rheumatic fever and subacute bacterial endocarditis may occur simultaneously in the same patient and even on the same valve.

Lemann has reported a case in which the disease developed in a mitral valve which had been made insufficient because of infarction of the left posterior papillary muscle due to a coronary artery thrombosis.

Of special interest is the association of subacute bacterial endocarditis with bicuspid aortic valves.

Congenital anomalies are next in importance to rheumatic deformities as predisposing factors of bacterial endocarditis.

The oldest patient we have seen was 74 and the youngest a child of 4. There is no significant predilection as regards sex, but in our experience males are affected somewhat more commonly.

Here and there one might like a little more ample discussion about details, and one might question whether a few of the cases quoted, particularly case 2 and case 3 on page 82, are sure instances of the disease with recovery. However, the volume can be wholeheartedly recommended.

The Story of Clinical Pulmonary Tuberculosis. By Lawrason Brown, M.D. Cloth. Price, $2.75. Pp. 411, with portrait. Baltimore: Williams & Wilkins Company, 1941.

For approximately two decades Dr. Lawrason Brown was regarded as the dean of authorities on clinical pulmonary tuberculosis in this country. Large numbers of tuberculous patients used his book entitled Rules for Recovery from Tuberculosis almost as their Bible. Medical audiences throughout the country listened to his addresses, and those who were fortunate enough to attend the Trudeau School of Tuberculosis reveled in his inspiring lectures on the history of clinical pulmonary tuberculosis. This new book will be heartily welcomed by the members of these various groups and by many other readers. The historical material presented is authentic, and Dr. Brown's own views and opinions are of great value, since he was a physician of unusually good judgment. It is particularly fitting that Dr. Homer L. Sampson should have contributed the chapter on x-rays, since it was he who was called almost from his bed as a patient in the Trudeau Sanatorium in 1912 to operate the first x-ray equipment installed in that institution. From that time to the present he has worked unceasingly at this post. No physician ever had a more loyal supporter and collaborator than Dr. Brown had in Dr. Sampson. In many ways and on numerous occasions Dr. Brown expressed his appreciation of Dr. Sampson's work. They labored together in learning how to improve the quality of the finished x-ray plate and film and how to interpret the shadows which it revealed. After the regular day's work they could be found in the x-ray laboratory, working until late at night to develop the roentgenographic phase of examination of the chest. Indeed, they inspected the plates and films of the chests of nearly half a million persons, and from their arduous work came numerous valuable contributions. Twenty years ago Dr. Brown manifested a great deal of enthusiasm for surgical methods in the treatment of pulmonary tuberculosis and was particularly loud in his praise of the splendid work of Dr. Edward W. Archibald of Montreal. They frequently conferred on this subject, and Dr. Brown referred patients to Dr. Archibald when he thought they would be benefited by surgical intervention. He recognized not only the great skill which Dr. Archibald possessed but his studious quality, which caused him to be regarded as one of the best informed chest surgeons in North America. Dr. Archibald's chapter, on the development of surgical methods in treatment, is an important contribution to the book. Dr. Brown spent many years compiling historical material on all phases of clinical pulmonary tuberculosis, and it is fortunate for the medical profession that this has been published in book form so that it will be preserved and available to physicians everywhere. An excellent bibliography is included.

Über Grundumsatz und Sexualhormone nach Kastration: Klinische und experimentelle Studien. Von E. Hart Hansen. Denne Afhandling er af det lægevidenskabelige Fakultet antaget til offentlig at forsvares for den medicinske Doktorgrad, København, 1940. Paper. Price, 12 Danish kroner. Pp. 211, with 30 illustrations. Copenhagen: Ejnar Munksgaard, 1941.

Denmark in 1929 was the first state in Europe to introduce castration into the modern administration of justice. There castrates are legally obliged to submit to examinations conducted by the medicolegal council. The problem of the author, who was awarded the opportunity to reexamine castrates in the Institute of Legal Medicine, was to observe (1) the occurrence of castration obesity in legally castrated men in Denmark, (2) the behavior of the basal metabolism in legally castrated persons, (3) the relation between castration obesity and changes in the basal metabolic rate, (4) the excretion of gonadotropin, estrogen and androgen in the urine after castration, (5) the effects produced on rats by the estrogen and androgen detected in the urine and (6) the relation between the results of the hormone analyses and of the determination of basal metabolism and the results observed in routine examinations. The author's conclusions were based on observations on 45 castrated persons, 24 ambulatory, 12 under institutional observation and 9 in an asylum for the feebleminded. Causes of castration were feebleminedness in 14 cases, psychopathy in 18, commitment to an institution in 12 and epilepsy in 1. His control material consisted of 14 healthy men, castrated women and men with other diseases.

Hansen found that castration obesity occurred in only 15.4 per cent of his subjects, proof that weight changes in male castrates are not ordinarily significant. The basal metabolic rate was less than 90 per cent in 6 of 38 castrates. No important information concerning reduced function of the male gonads was revealed by the basal metabolism examinations. Castration obesity and decreased metabolism did not run parallel. Of 38 subjects examined, 1 with castration obesity and 4 without castration obesity showed a decreased basal metabolic rate; 5 with castration obesity and 28 without castration obesity were without a decrease in the rate. An increased excretion of sex hormone occurred after castration of men. Estrogen excretion was less in noncastrated men than in those who had been castrated. The urine of men contained smaller amounts of estrogen than that of women. In general, castrates excreted smaller amounts of androgen in the urine than normal men. Improved methods resulted in an increase in the amount of androgen which could be detected. Injections of androgen into castrated male rats produced an increase in weight of the prostate, the seminal vesicles and the penis. Injections of estrogen into female castrated rats caused doubling of the weight of the vagina and cervix. The results of the preceding experiments were compared with parallel experiments with androsterone in capons.

The author found no difference in the relationship between the results obtained in the determination of the basal metabolic rate and the results of the hormone analysis in subjects with a rate less than 90 per cent and those with a rate greater than 90 per cent. Obesity did not influence the results. These data, while of no value in reexamination of the individual, are in no wise derogatory to the application of castration on a legal basis. The hormone balance of the organism is influenced by postpuberal castration. This is evident from the increased excretion of gonadotropin and the decreased excretion of androgen and estrogen in the urine. The author states that this investigation has revealed no causal connection between androgen secretion and the remains of libido and potency of castrates.

It may be assumed that a metabolism of substances (related to cholesterol and provided with sex hormone properties) takes place in the organism. These substances exert a specific influence on the morphology and function of the secondary sex characters. This metabolism is under the influence of the gonads but does not stop after castration. Finally, the importance of such scientific investigations in a state such as Denmark, where castration is on a legal basis, is stressed.

Chinese Lessons to Western Medicine: A Contribution to Geographical Medicine from the Clinics of Peiping Union Medical College. By I. Snapper, Professor and Head of the Department of Medicine, Peiping Union Medical College, Peiping. With a foreword by George R. Minot, Professor of Medicine, Harvard University, Boston. Cloth. Price, $5.50. Pp. 380, with 132 illustrations. New York: Interscience Publishers, Inc., 1941.

This book, written in a breezy, narrative style, does not purport to be a systematic study of the diseases characteristic of North China but is rather a record of the impressions of the author, a Dutch clinician with a worldwide reputation, during the first two years following his transplantation to the Peiping Union Medical College. These impressions are, however, in most instances carefully documented from the hospital records and are supported by many excellent illustrations and detailed case records.

Although Peiping is situated at a latitude of 40 north, about the same as that of Philadelphia, its diseases are largely tropical or semitropical, and one is struck, on first visiting the wards of the Peiping Union Medical College Hospital, with the preponderance of patients with acute infectious disorders. Dr. Snapper thus gives due prominence to relapsing fever, typhus and amebiasis, all of which lend color to the practice of medicine in China, but even more to kala-azar, the parasitic disease which places its mark all over internal medicine in North China and which is so frequent that it has to be considered in nearly every case.

The manifestations of cardiovascular disease in North China are considered in detail, and one of the common myths about China, i. e. that the Chinese, owing to the placidity of their dispositions, are not subject to hypertension, is disposed of. Essential hypertension, both benign and malignant, is common. Arteriosclerosis, however, with the syndrome of angina pectoris and with coronary occlusion and myocardial infarction, is rare, and Dr. Snapper speculates about the relationship of the low cholesterol intake and the consequent low blood cholesterol concentrations in the Chinese to the reduced tendency to lipoid infiltration of the blood vessel wall, pointing out at the same time the relatively high figures for the unsaturated fatty acids, especially linoleic and linolenic acids.

There is an extended consideration of the anemias, concluding with the statement that, while macrocytic nutritional anemia is frequent, genuine pernicious anemia rarely occurs. Dr. Snapper also calls attention to the prevalence of diabetes mellitus and rickets, without noting that it used to be said of these disorders, as of hypertension, that they did not occur in China. With the establishment of the Peiping Union Medical College and of its hospital, to which Dr. Snapper refers as now one of the best modern teaching hospitals, the search for these conditions really began, and they appeared with about the same frequency as in the United States.

It is pointed out that every phase of clinical medicine in Peiping is influenced by the peculiar food situation, which leads to general undernutrition, with deficiencies of all the vitamins except those of the B complex. In North China the B complex vitamins are provided by the relatively large intake of a coarse, whole ground millet, in contrast to the diet of polished rice common farther south.

The book should be required reading for any one whose attention, for any reason, is being drawn to the problems of medicine in the Orient.

Xanthoma and Other Dyslipoidoses. By Fred D. Weidman, M.D., L. Napoleon Boston, M.D., Joseph Stokes, Jr., M.D., Howard W. Schaffer, M.D., Walter Freeman, M.D., and F. W. Sunderman, M.D. [Including Reprinted Articles from the Archives of Dermatology and Syphilology, Archives of Internal Medicine, American Journal of Diseases of Children and Archives of Surgery.] Cloth. Price, $3. Pp. 195, with illustrations. Philadelphia: University of Pennsylvania Press, 1941.

In the introduction Weidman knits the thoughts that prompted these papers and their grouping and stresses the significance of "xanthoses and lipoid disturbances, related diffuse conditions and the growth in knowledge which has been so remarkable that nearly every branch of medicine has become involved to a greater or lesser extent by its ramifications: dermatology, internal medicine, surgery, ophthalmology, pediatrics, otolaryngology, stomatology, physiologic chemistry and pathology." The book contains an index aimed to correlate the biologic phases of xanthoma, particularly the pathologic data, and an article on the pathology of the yellowing dermatoses which is useful from the clinical angle because it will assist in the differential diagnosis of certain of its members from the xanthoma group. This work is recommended to all practitioners in medicine for its excellence and the broad scope of its correlation of xanthoma as a possible manifestation of a medical entity in the skin. The enlarged concept of dermatology, including xanthoma, acute disseminated lupus erythematosus (Libman-Sacks syndrome), the purpuras, tuberculids, drug eruptions and the lymphoblastomas easily fulfil their relationship to medicine in general as cutaneous medicine.

Semiologia do ovário com um estudo particular da citologia vaginal pelo método de Shorr. Pelo Dr. Francisco Victor Rodrigues, professor de clínica ginecológica da Faculdade fluminense de medicina, Rio de Janeiro. Cloth. Pp. 286, with 35 illustrations. Rio de Janeiro: A Casa do Livro Limitada, 1941.

This is an excellent study based on the literature and presenting first the embryology, anatomy, pathology and physiology of the ovaries, with few illustrations. After this portion the author goes into the chief material of the volume, which might better be entitled the functional examination of the ovaries. (The author does not include the direct physical examination of the ovaries, as the Portuguese title would suggest.) This is illuminated by detailed studies of 36 of his own cases, including a number of excellent illustrations, some colored, especially of the vaginal smear method of Papanicolaou and Shorr, which the author interprets correctly and makes much use of. In addition to an extensive bibliography which shows an appreciation of the world literature up until late in 1941 the author includes the list of his publications in this general field of gynecology.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

RENAL CALCULI AND SULFONAMIDES

To the Editor:—**The question of sulfonamide derivatives causing renal calculi has come to my attention recently through the queries of patients and I would appreciate information on the following: Does the formation of renal calculi have any bearing on the administration of sulfonamide drugs? If so, does the drug predispose to the formation of the usual type of stone or do the crystals of the drug collect to form a foreign body in the kidney pelvis? Does the dose of the sulfonamide drug influence the formation of calculi? And, if renal calculi existed before the administration of the drug, would the drug aggravate the condition? If the sulfonamide drugs do form renal calculi, are they permanent or are they dissolved after withdrawal of the drug? What drug of the sulfonamide group is most likely to form crystals in the urine and possibly assemble in the kidney pelvis to form a foreign body visible by x-ray examination? Does the administration of iodized oil for bronchography have any therapeutic value; if so, what and for what?**

Louis S. Miles, M.D., Summerville, S. C.

ANSWER.—We have no evidence which would indicate that the sulfonamide drugs bear any relation to the formation of renal calculi, either by predisposing toward, or aggravating, existing calculi. The so-called crystals of the drug do not form calculi in the sense with which we usually associate that term; rather they form needles or crystals which in themselves may cause damage or which may "coalesce" to result in larger bodies. Perhaps some consider these larger bodies as calculi, but the term would be a misnomer.

The crystalline bodies which may form following the use of certain sulfonamides tend to disappear on withdrawal of the drug or following the forcing of fluids. However, there are records of necropsies which have shown the masses too large for excretion by the ordinary channels. This explains why so much attention is given to daily examination of the urine when sulfonamide therapy is in progress.

Information does not appear to be available as to the visibility of these bodies by x-ray technic.

The drug which would most likely form crystals in the urine is sulfapyridine.

We have no evidence of any therapeutic value associated with the administration of iodized oil for bronchography.

STERILITY DETECTORS—DIACK CONTROL, STERILOMETER AND ASEPTIC-THERMO INDICATOR

To the Editor:—**What products are considered reliable for determining the sterility of autoclaved materials?**

Ansel Woodburn, M.D., Urbana, Ohio.

ANSWER.—A number of devices designed to indicate whether or not materials in autoclaves have been sterilized are on the market and in common use. Three of these in particular have been the subject of numerous investigations. The Diack Control is a small sealed glass tube containing a reddish crystalline substance which is supposed to melt or fuse and change color at 121 C. Obviously this reaction is largely or entirely dependent on the single factor of temperature. The Sterilometer is a thermometer-like drawing on a square piece of cardboard; the bulb of the thermometer is said to turn black promptly on exposure to moist heat, and the stem to turn black after subjection to steam at 110 to 120 C. for fifteen minutes, i. e. under conditions which insure destruction of all micro-organisms including the spore formers. The Aseptic-Thermo Indicator, which is similar in principle, has a lavender arrow on a green dial pointing to the figure 250°; under the conditions of heat and moisture just described the arrow turns green so as to match its background.

In 1933 T. B. Magath reported a study of Aseptic-Thermo Indicator (*Mod. Hosp.* **41**:112 [Sept.] 1933) in which twenty-five of these devices were tested and were found to turn green only after exposure to 121 C. for twenty minutes. The conclusion drawn was that these indicators are satisfactory for testing sterilization with steam under pressure for all uses in bacteriologic laboratories and hospitals. A further investigation of these products was carried out under the auspices of the A. M. A. Chemical Laboratory (THE JOURNAL, Nov. 24, 1934, p. 1621). Both the Sterilometer and the Thermo Indicator were found to be efficient in determining sterilization by the autoclave. It was felt that neither type could cause a false sense of security, since whenever the reaction or change was irregular the change was on the side of safety and failure of matching.

These opinions were not corroborated by subsequent investigations, however. Quigley at Johns Hopkins Hospital after extensive studies concluded that the three devices are all unreliable, and their use in that institution was discontinued forthwith (personal communication). Underwood, whose book (A Textbook of Disinfection, Erie, Pa., American Sterilizer Company, 1934) is based on investigations carried out in several leading medical centers, contended that none of these indicators are fully trustworthy, although of the three types the Diack Control is the most uniform and generally satisfactory. Underwood cites the work of Ecker, who found that Diack controls fuse at 122 C. in two minutes, at 118 C. in five to ten minutes and at 115 C. in ten to fifteen minutes; that sterilometers change color with the least exposure to steam, the color becoming black with high temperatures, intermediate changes of color being variable and difficult to interpret correctly; and that Aseptic-Thermo indicators show no color changes short of 124 C. for fifteen minutes or 121 C. for twenty minutes, this requirement being too high since it spoils rubber goods and dextrose solutions. Underwood criticized pasteboard indicators because they show some color changes at less than regulation temperatures, because the color fades somewhat in sunlight, because any hydrogen sulfide gas present may cause misleading color changes (in sterilometers), because the degree of color change requires interpretation and thus adds a factor of uncertainty, and because the cards cannot be extracted from the centers of packages without disturbing the covers and contaminating the contents.

The most damaging evidence against these telltale indicators was submitted by C. W. Walter (*Surgery* **2**:582 [Oct.] 1937), who tested one thousand each of the three types. A glass steam pressure chamber was used so that the products could be observed constantly under controlled conditions of temperature, pressure and moisture. Walter found that there were discrepancies between individual Diack controls, that they melt equally in dry and moist heat, and that most of the samples melt in one minute or less at the usual sterilizing temperatures, although in some tests melting was delayed longer than the time usually required for sterilization. Sterilometers were found to have an extremely poor end point of color change. Most of the samples of this product showed complete blackening in less than six minutes, the average time being well below the advertised and published claims; some, however, showed delayed color changes which in practice might have resulted in unnecessary resterilization of the loads. Aseptic-Thermo indicators likewise had poor end points, the majority of samples changing color in less than twelve minutes, although in some change was unduly delayed. On the whole, the indicators were found to be the most consistent of the three types of devices. Walter concluded that the expense of using telltale indicators to certify sterility is not justified because of disparity in individual performance and that the large personal equation in placing and interpreting them makes their use of doubtful value in general hospital practice.

Concerning these devices, Elliott C. Cutler says editorially (*Surg., Gynec. & Obst.* **67**:531 [Oct.] 1938) "Various sterility detectors have been devised to assure the surgeon sterile supplies, but such detectors have proved inadequate."

Other methods have been utilized in the effort to insure sterilization by autoclaves. Maximum thermometers proved unpractical, since they cannot be placed conveniently inside representative packages of material and since they give no indication of how long the maximal temperature has been maintained. It has been suggested that a thermometer be placed in the discharge line of autoclaves in the belief that the temperature in the sterilizing chamber is certain to be as high as or higher than it is in the exhaust pipe. Timing in such a case should commence when the escaping steam has reached the standard sterilizing temperature (e. g. 121 C.). This is a simple method which has much to recommend it. The most satisfactory and reliable detector thus far devised is the recording potentiometer. Thermocouples placed inside representative packages in the autoclave lead to an instrument which records continuously on a time chart the temperatures inside those packages. By this means the desired temperature for the desired length of time inside all the bundles of a load can be virtually assured. Unfortunately these recording potentiometers are rather expensive. For the sterilizing departments of large hospitals an apparatus of proved worth is "Micromax," a multiple recording potentiometer with as many as eight leads,

manufactured by Leeds and Northrop Company, Philadelphia. Walter (*ibid.* **67**:526 [Oct.] 1938) has described a control mechanism to be used in connection with a potentiometer which automatically locks the door of the autoclave until standards of sterilization have been met. He claims that this apparatus can be used to eliminate "faulty sterilization due to failure of the sterilizing equipment and ignorance or negligence on the part of the attendant."

It must not be thought, however, that the problem of steam sterilization has been fully solved or that any fool proof method of carrying out the procedure has been discovered. The basic requirement for certain and satisfactory sterilization is that every part of the load, even the center of large, dense packages, should be subjected to moist heat of 121-126 C. for more than fifteen minutes or 115-121 C. for more than twenty minutes, conditions which are known to kill the most resistant microorganisms. The main difficulty lies in adequate expulsion of air from the autoclave chamber and avoidance of pockets of air inside glass jars, rubber gloves and bundles of fabric. Steam and air mix slowly, and diffusion of heat from steam to air requires time. Even after sufficient steam has entered the sterilizer to raise the pressure gage to 15 pounds, air pockets may for a long time show substandard degrees of temperature and moisture. Pressure gages are untrustworthy, therefore, for the purpose of timing steam sterilization, since it is moist heat, not pressure, which kills the bacteria. The best indicator, as has been pointed out, is a recording potentiometer with leads inside large, dense packages and other places where air is apt to pocket or where penetration of steam may be delayed, and the timing of the period of sterilization should not begin until the temperatures in those regions has reached the predetermined standard. Ideally there should be a companion device to indicate whether the heat in those regions is sufficiently moist, since dry heat of 121 C. or less may not kill all the organisms. Some idea of the degree of penetration of steam to the thermocouples can be obtained, however, by noting the lapse of time between closure of the discharge line of the autoclave and the registering of 121 C. by the potentiometer. Ordinarily this requires less than twenty-two minutes (Quigley). If this rise in temperature requires more than twenty-two minutes, it is presumptive evidence that penetration has been delayed unduly and that dangerous pocketing of air has occcurred which requires reexamination of the load and a fresh attempt to expel air from the sterilizer.

In conclusion it should be emphasized that pressure steam sterilization cannot be assured without intelligent and conscientious attention to the rules which govern preparation of packages, assemblying of loads and operation of the autoclave. Sterility detectors should be viewed as stimulants and correctives, not as substitutes for careful work on the part of the attendant.

CHILBLAINS

***To the Editor:*—I have been given the following history concerning a woman aged 26 whom I have not seen and who lives in a cold climate: "When she was a little girl her shins were frozen and now in cold weather the shins become red, chap easily and hurt some. In very cold weather they may bleed a little." In your opinion is it possible for these symptoms to be due to "freezing of the shins" twenty years ago?**

M.D., California.

ANSWER.—This young woman probably has chilblains or erythema pernio, which usually affects the extremities of subjects with poor peripheral circulation. It appears as various shades of red and purple infiltrated patches and plaques, which are tender and itch or burn, and, characteristically, cold weather incites their presence. The parts are cool to the touch, and the redness disappears on pressure. The manifestations tend to disappear in the warmer seasons. The disease is most prevalent in damp, cold climates. It affects people with the so-called chilblain circulation, which is feeble and is sometimes denoted by cold hands and feet.

In some cases chilblains and its background of impaired circulation becomes difficult to distinguish from livedo reticularis of the extremities, acrocyanosis and erythrocyanosis. A dusky reddish appearance may be imparted by permanently dilated superficial blood vessels, giving a reticulated and marbled pattern. Such changes in the vessels can be produced by syphilis, tuberculosis and toxemias; anomalies of the blood vessels and arteriosclerosis as well as infectious processes may be other causes. A tuberculous background not infrequently may be present in those with poor circulation and subject to frostbite.

Simple pernio needs to be differentiated from lupus pernio, which is a type of sarcoidosis. The latter is a manifestation of tuberculosis, a large number of observers believe. It manifests itself as erythematous symmetrical areas that are infiltrated and thickened. They vary in color but are often a type of bluish red. They may have dilated blood vessels coursing over them. The diagnosis is readily made by microscopic examination. The tissue has a characteristic appearance. The treatment is with arsenical and gold administrations and exposure to roentgen rays. This type of lupus pernio is the so-called Besnier variety, probably due to tuberculosis.

A second variety of lupus pernio, the Hutchinson type, or chilblain lupus, is a manifestation of lupus erythematosus. This consists of infiltrated erythematous patches and plaques which are aggravated in cold weather. The lesions occur on the face and extremities. Early they look like chilblains but later become more infiltrated and permanent and then look like lupus erythematosus. This type lacks the brownish nodules seen in the Besnier type when viewed through a glass pressed against the surface. Later the plaques are bluish or violaceous and scale, and finally they show atrophy, beginning first at the center. The histologic changes are those found in lupus erythematosus. The greatest difficulty in distinguishing these lesions from ordinary frostbite is present early before tumefaction occurs. Ordinarily, however, chilblains disappears in warm weather, but lupus pernio continues on, though the latter is worse in the winter.

The treatment of chilblains is by attention to the health in general. A tuberculous background, for example, may be present. The circulation should be improved with exercise and locally by friction and massage. Camphor liniment or bay rum may be applied. The extremities may be covered thoroughly with talcum and wrapped in cotton wool held in place by a bandage. The extremities should be kept warm continuously. The administration of arsenic before cold weather sets in is considered prophylactic. The cautious use of acetylcholine and related materials locally as by iontophoresis may be considered as of the newer remedies and not entirely evaluated at present.

ULTRAVIOLET BURNS OF THE EYE

***To the Editor:*—With the expansion of the heavy industries the number of cases of ultraviolet burns of the eye has greatly increased. Can any curative substances be used locally in the eye in such cases?**

Jonas S. Friedenwald, M.D., Baltimore.

ANSWER.—Inflammation of the eye caused by ultraviolet rays involves only the cornea, causing a characteristic photophthalmia. Only the epithelial cells are involved, although in prolonged exposure the superficial substantia propria may be attacked. The corneal surface is stippled, slightly at first, but, as the latent photochemical reactions develop, the individual epithelial cells extrude their nuclei and finally desquamate. The entire process is characterized by extreme rapidity of cell death and of cell regeneration.

In the beginning of an attack of photophthalmia, iced applications are of some value. One of the more recent corneal anesthetics afford relief, but cocaine is contraindicated. An antiseptic agent to prevent infection of the eroded areas is of definite value. After twenty-four hours, heat hastens epithelial regeneration. There are no known therapeutic agents of curative value; but the condition is self limited, provided there is no intercurrent infection of the corneal surface. (See Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, C. V. Mosby Company **1**:818.)

PHLEBITIS AND CHILDBIRTH

***To the Editor:*—A patient who has a child nearly 4 years old now desires another. She tells me that she had a severe phlebitis following this birth and wishes to know the possibility of this occurring again. What should be advised?**

M.D., Maine.

ANSWER.—Roughly speaking, an involvement of the veins of the lower extremities trebles the incidence of postoperative thrombosis and embolism after abdominal hysterectomy (Barker, N. W.; Nygaard, K. K.; Walters, Waltman, and Priestley, J. T.: *Proc. Staff Meet., Mayo Clin.* **16**:33 [Jan. 15] 1941). As a collective review of 179,072 childbirths gave an incidence of 1.3 per cent of thrombosis (Nurnberger, L.: *Verhandl. d. deutsch. Gesellsch. f. Kreislaufforsch.*, p. 101, 1934), a previous thrombosis might approximately result by analogy in a 4 per cent incidence of thrombosis. The patient, then, is taking about the same chance as if she were undergoing an abdominal hysterectomy instead of a childbirth *per vias naturales.*

Cardiac disease, obesity, age above 40, prolonged labor, dehydration, anemia and infection are other predisposing factors. Elevation of the foot of the bed, snug bandaging of the limbs and cautious administration of heparin for seven to ten days after delivery will minimize the recurrence of phlebitis.